

SAS/STAT® 9.22 User's Guide The LIFETEST Procedure (Book Excerpt)



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Chapter 49

The LIFETEST Procedure

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Overview: LIFETEST Procedure

A common feature of lifetime or survival data is the presence of right-censored observations due either to withdrawal of experimental units or to termination of the experiment. For such observations, you know only that the lifetime exceeded a given value; the exact lifetime remains unknown. Such

data cannot be analyzed by ignoring the censored observations because, among other considerations, the longer-lived units are generally more likely to be censored. The analysis methodology must correctly use the censored observations as well as the uncensored observations.

Texts that discuss the survival analysis methodology include Collett (1994), Cox and Oakes (1984), Kalbfleisch and Prentice (1980), Klein and Moeschberger (1997), Lawless (1982), and Lee (1992). Users interested in the theory should consult Fleming and Harrington (1991) and Andersen et al. (1992).

Usually, a first step in the analysis of survival data is the estimation of the distribution of the survival times. Survival times are often called *failure* times, and *event* times are uncensored survival times. The survival distribution function (SDF), also known as the survivor function, is used to describe the lifetimes of the population of interest. The SDF evaluated at t is the probability that an experimental unit from the population will have a lifetime exceeding t—that is,

$$S(t) = \Pr(T > t)$$

where S(t) denotes the survivor function and T is the lifetime of a randomly selected experimental unit. The LIFETEST procedure can be used to compute nonparametric estimates of the survivor function either by the product-limit method (also called the Kaplan-Meier method) or by the life-table method (also called the actuarial method). The life-table estimator is a grouped-data analog of the Kaplan-Meier estimator. The procedure can also compute the Breslow estimator or the Fleming-Harrington estimator, which are asymptotic equivalent alternatives to the Kaplan-Meier estimator.

Some functions closely related to the SDF are the cumulative distribution function (CDF), the probability density function (PDF), and the hazard function. The CDF, denoted F(t), is defined as 1 - S(t) and is the probability that a lifetime does not exceed t. The PDF, denoted f(t), is defined as the derivative of F(t), and the hazard function, denoted h(t), is defined as f(t)/S(t). If the life-table method is chosen, the estimates of the probability density function can also be computed. Plots of these estimates can be produced by a graphical or line printer device, or based on the output delivery system (ODS).

An important task in the analysis of survival data is the comparison of survival curves. It is of interest to determine whether the underlying populations of k ($k \ge 2$) samples have identical survivor functions. PROC LIFETEST provides nonparametric k-sample tests based on weighted comparisons of the estimated hazard rate of the individual population under the null and alternative hypotheses. Corresponding to various weight functions, a variety of tests can be specified, which include the log-rank test, Wilcoxon test, Tarone-Ware test, Peto-Peto test, modified Peto-Peto test, and Fleming-Harrington G_{ρ} family of tests. PROC LIFETEST also provides corresponding trend tests to detect ordered alternatives. Stratified tests can be specified to adjust for prognostic factors that affect the events rates in the various populations. A likelihood ratio test, based on an underlying exponential model, is also included to compare the survival curves of the samples.

There are other prognostic variables, called covariates, that are thought to be related to the failure time. These covariates can also be used to construct statistics to test for association between the covariates and the lifetime variable. PROC LIFETEST can compute two such test statistics: censored data

linear rank statistics based on the exponential scores and the Wilcoxon scores. The corresponding tests are known as the log-rank test and the Wilcoxon test, respectively. These tests are computed by pooling over any defined strata, thus adjusting for the stratum variables.

One change in SAS 9.2 is that the calculation of confidence limits for the quartiles of survival time is based on the transformation specified by the CONFTYPE= option. Another change is that the SURVIVAL statement in SAS 9.1 is folded into the PROC LIFETEST statement; that is, options that were in the SURVIVAL statement can now be specified in the PROC LIFETEST statement. The SURVIVAL statement is no longer needed and it is not documented.

Getting Started: LIFETEST Procedure

You can use the LIFETEST procedure to compute nonparametric estimates of the survivor functions, to compare survival curves, and to compute rank tests for association of the failure time variable with covariates.

For simple analyses, only the PROC LIFETEST and TIME statements are required. Consider a sample of survival data. Suppose that the time variable is T and the censoring variable is C with value 1 indicating censored observations. The following statements compute the product-limit estimate for the sample:

```
proc lifetest;
   time t*c(1);
run;
```

You can use the STRATA statement to divide the data into various strata. A separate survivor function is then estimated for each stratum, and tests of the homogeneity of strata are performed. However, if the GROUP= option is also specified in the STRATA statement, the GROUP= variable is used to identify the samples whose survivor functions are to be compared, and the STRATA variables are used to define the strata for the stratified tests. You can specify covariates (prognostic variables) in the TEST statement, and PROC LIFETEST computes linear rank statistics to test the effects of these covariates on survival.

For example, consider the results of a small randomized trial on rats. Suppose you randomize 40 rats that have been exposed to a carcinogen into two treatment groups (Drug X and Placebo). The event of interest is death from cancer induced by the carcinogen. The response is the time from randomization to death. Four rats died of other causes; their survival times are regarded as censored observations. Interest lies in whether the survival distributions differ between the two treatments.

The following DATA step creates the data set Exposed, which contains four variables: Days (survival time in days from treatment to death), Status (censoring indicator variable: 0 if censored and 1 if not censored), Treatment (treatment indicator), and Sex (gender: F if female and M if male).

```
proc format;
   value Rx 1='Drug X' 0='Placebo';
data exposed;
  input Days Status Treatment Sex $ @@;
  format Treatment Rx.;
  datalines;
          1
              F
                   378
                         0
                             1
179
      1
                                 М
256
      1
          1
              F
                   355
                         1
                             1
                                 М
                   319
                             1
262
      1
          1
              М
                         1
                                 М
256
          1
              F
                   256
                             1
                                 М
      1
                         1
                             1
255
      1
          1
              М
                   171
                         1
                                 F
224
      0
          1
              F
                   325
                         1
                             1
                                 М
225
      1
          1
              F
                   325
                         1
                             1
                                 М
287
      1
          1
              М
                   217
                         1
                             1
                                 F
                             1
319
      1
          1
              M
                   255
                         1
                                 F
                   256
                             1
                                 F
264
      1
          1
              M
                         1
237
      0
          0
              F
                   291
                         1
                             0
                                 М
156
      1
          0
              F
                   323
                         1
                             0
                                 М
270
      1
          0
              М
                   253
                         1
                             0
                                 М
257
          0
              М
                   206
                         1
                             0
                                 F
                             0
          0
                   206
                                 F
242
      1
              M
                         1
          0
              F
                   237
                         1
                             0
157
      1
                                 М
          0
                             0
                                 F
249
      1
              M
                  211
                         1
180
      1
          0
              F
                   229
                         1
                             0
                                 F
          0
              F
                   234
                             0
                                 F
226
      1
                         1
          0
                   209
                             0
                                 F
268
;
```

PROC LIFETEST is invoked as follows to compute the product-limit estimate of the survivor function for each treatment and to compare the survivor functions between the two treatments.

```
ods graphics on;
proc lifetest data=Exposed plots=(survival(atrisk) logsurv);
   time Days*Status(0);
   strata Treatment;
run;
ods graphics off;
```

In the TIME statement, the survival time variable, Days, is crossed with the censoring variable, Status, with the value 0 indicating censoring. That is, the values of Days are considered censored if the corresponding values of Status are 0; otherwise, they are considered as event times. In the STRATA statement, the variable Treatment is specified, which indicates that the data are to be divided into strata based on the values of Treatment. Graphics results are enabled through ODS with the specification of the ODS GRAPHICS ON statement. Two plots are requested through the PLOTS= option—a plot of the survival curves with at risk numbers and a plot of the negative log of the survival curves.

The results of the analysis are displayed in the following figures.

Figure 49.1 displays the product-limit survival estimate for the Drug X group (Treatment=1). The figure lists, for each observed time, the survival estimate, failure rate, standard error of the estimate, cumulative number of failures, and number of subjects remaining in the study.

Figure 49.1 Survivor Function Estimate for the Drug X-Treated Rats

Stratum 1: Treatment = Drug X							
	Produc	t-Limit Surv	ival Estimat	es			
			Survival Standard	Number	Number		
Days	Survival	Failure	Error	Failed	Left		
0.000	1.0000	0	0	0	20		
171.000	0.9500	0.0500	0.0487	1	19		
179.000	0.9000	0.1000	0.0671	2	18		
217.000	0.8500	0.1500	0.0798	3	17		
224.000*			•	3	16		
225.000	0.7969	0.2031	0.0908	4	15		
255.000			•	5	14		
255.000	0.6906	0.3094	0.1053	6	13		
256.000			•	7	12		
256.000			•	8	11		
256.000			•	9	10		
256.000	0.4781	0.5219	0.1146	10	9		
262.000	0.4250	0.5750	0.1135	11	8		
264.000	0.3719	0.6281	0.1111	12	7		
287.000	0.3187	0.6813	0.1071	13	6		
319.000		•		14	5		
319.000	0.2125	0.7875	0.0942	15	4		
325.000		•		16	3		
325.000	0.1062	0.8938	0.0710	17	2		
355.000	0.0531	0.9469	0.0517	18	1		
378.000*	0.0531			18	0		

Figure 49.2 displays summary statistics of survival times for the Drug X group. It contains estimates of the 25th, 50th, and 75th percentiles and the corresponding 95% confidence limits. The median survival time for rats in this treatment is 256 days. The mean and standard error are also displayed; however, it is noted that these values are underestimated because the largest observed time is censored and the estimation is restricted to the largest event time.

Figure 49.2 Summary Statistics of Survival Times for Drug X-Treated Rats

Quartile Estimates					
	Point	95% Co	nfidence Inte	erval	
Percent	Estimate	Transform	[Lower	Upper)	
75	319.000	LOGLOG	256.000	355.000	
50	256.000	LOGLOG	255.000	319.000	
25	255.000	LOGLOG	171.000	256.000	

Figure 49.2 continued

 Mean
 Standard Error

 271.131
 11.877

NOTE: The mean survival time and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time.

Figure 49.3 and Figure 49.4 display the survival estimates and the summary statistics of the survival times for Placebo (Treatment=0). The median survival time for rats in this treatment is 235 days.

Figure 49.3 Survivor Function Estimate for Placebo-Treated Rats

The LIFETEST Procedure

Stratum 2: Treatment = Placebo

Product-Limit Survival Estimates

Days	Survival	Failure	Survival Standard Error	Number Failed	Number Left
0.000	1.0000	0	0	0	20
156.000	0.9500	0.0500	0.0487	1	19
157.000	0.9000	0.1000	0.0671	2	18
180.000	0.8500	0.1500	0.0798	3	17
206.000				4	16
206.000	0.7500	0.2500	0.0968	5	15
209.000	0.7000	0.3000	0.1025	6	14
211.000	0.6500	0.3500	0.1067	7	13
226.000	0.6000	0.4000	0.1095	8	12
229.000	0.5500	0.4500	0.1112	9	11
234.000	0.5000	0.5000	0.1118	10	10
237.000	0.4500	0.5500	0.1112	11	9
237.000*			•	11	8
242.000	0.3938	0.6063	0.1106	12	7
249.000	0.3375	0.6625	0.1082	13	6
253.000	0.2813	0.7188	0.1038	14	5
257.000	0.2250	0.7750	0.0971	15	4
268.000*			•	15	3
270.000	0.1500	0.8500	0.0891	16	2
291.000	0.0750	0.9250	0.0693	17	1
323.000	0	1.0000		18	0

NOTE: The marked survival times are censored observations.

Figure 49.4 Summary Statistics of Survival Times for Placebo-Treated Rats

	Point	95% Co	nfidence Int	erval		
Percent	Estimate	Transform	[Lower	Upper)		
75	257.000	LOGLOG	237.000	323.000		
50	235.500	LOGLOG	206.000	253.000		
25	207.500	LOGLOG	156.000	229.000		
Mean Standard Error						

A summary of the number of censored and event observations is shown in Figure 49.5. The figure lists, for each stratum, the number of event and censored observations, and the percentage of censored observations.

Figure 49.5 Number of Event and Censored Observations

Summ	ary of the Number	of Cen	sored and	Uncensored	Values
					Percent
Stratum	Treatment	Total	Failed	Censored	Censored
1	Drug X	20	18	2	10.00
2	Placebo	20	18	2	10.00
Total		40	36	4	10.00

Figure 49.6 displays the graph of the product-limit survivor function estimates versus survival time. The two treatments differ primarily at larger survival times. Note the number of subjects at risk in the plot. You can display the number of subjects at risk at specific time points by using the ATRISK= option.

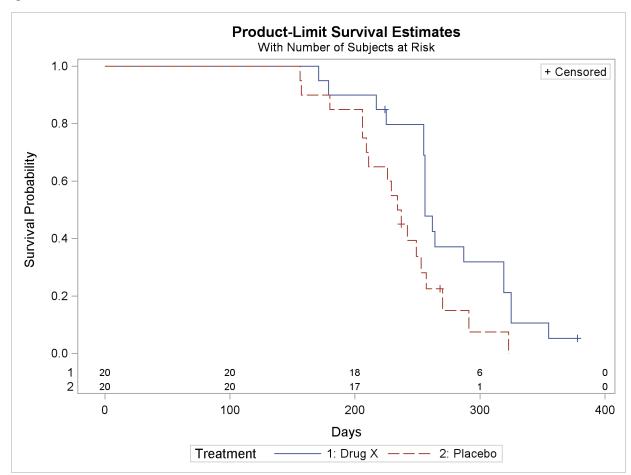


Figure 49.6 Plot of Estimated Survivor Functions

Figure 49.7 displays the graph of the log survivor function estimates versus survival time. Neither curve approximates a straight line through the origin—the exponential model is not appropriate for the survival data.

Note that these graphical displays are generated through ODS. For general information about ODS Graphics, see Chapter 21, "Statistical Graphics Using ODS."

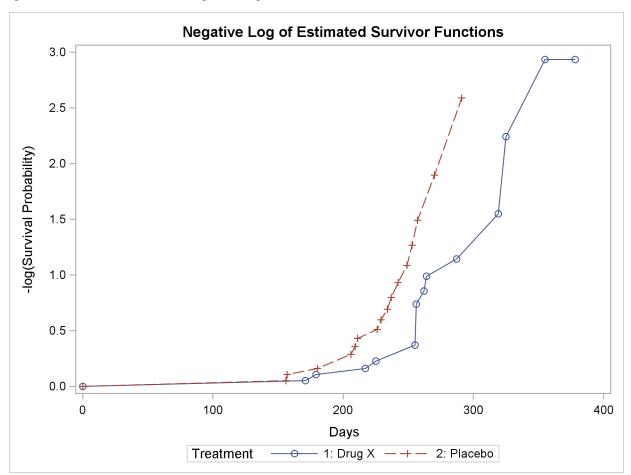


Figure 49.7 Plot of Estimated Negative Log Survivor Functions

Results of the comparison of survival curves between the two treatments are shown in Figure 49.8. The rank tests for homogeneity indicate a significant difference between the treatments (p=0.0175 for the log-rank test and p=0.0249 for the Wilcoxon test). Rats treated with Drug X live significantly longer than those treated with Placebo. Since the survival curves for the two treatments differ primarily at longer survival times, the Wilcoxon test, which places more weight on shorter survival times, becomes less significant than the log-rank test. As noted earlier, the exponential model is not appropriate for the given survival data; consequently, the result of the likelihood ratio test should be ignored.

Figure 49.8 Results of the Two-sample Tests

Т	Test of Equality over Strata					
			Pr >			
Test	Chi-Square	DF	Chi-Square			
Log-Rank	5.6485	1	0.0175			
Wilcoxon	5.0312	1	0.0249			
-2Log(LR	0.1983	1	0.6561			

Next, suppose male rats and female rats are thought to have different survival rates, and you want to assess the treatment effect while adjusting for the gender differences. By specifying the variable Sex in the STRATA statement as a stratifying variable and by specifying the variable Treatment in the GROUP= option, you can carry out a stratified test to test Treatment while adjusting for Sex. The test statistics are computed by pooling over the strata defined by the values of Sex, thus controlling for the effect of Sex. The NOTABLE option is added to the PROC LIFETEST statement as follows to avoid estimating a survival curve for each gender.

```
proc lifetest data=Exposed notable;
  time Days*Status(0);
  strata Sex / group=Treatment;
run;
```

Results of the stratified tests are shown in Figure 49.9. The treatment effect is statistically significant for both the log-rank test (p=0.0071) and the Wilcoxon test (p=0.0150). As compared to the results of the unstratified tests in Figure 49.8, the significance of the treatment effect has been sharpened by controlling for the effect of the gender of the subjects.

Figure 49.9 Results of the Stratified Two-Sample Tests

```
The LIFETEST Procedure

Stratified Test of Equality over Group

Pr >

Test Chi-Square DF Chi-Square

Log-Rank 7.2466 1 0.0071
Wilcoxon 5.9179 1 0.0150
```

Since Treatment is a binary variable, another way to study the effect of Treatment is to carry out a censored linear rank test with Treatment as an independent variable. Although this test is less popular than the two-sample test, nevertheless, in situations where the independent variables are continuous and are difficult to discretize, it might be infeasible to perform a *k*-sample test. To compute the censored linear rank statistics to test the Treatment effect, Treatment is specified in the TEST statement as follows.

```
proc lifetest data=Exposed notable;
  time Days*Status(0);
  test Treatment;
run;
```

Results of the linear rank tests are shown Figure 49.10. The *p*-values are very similar to those of the two-sample tests in Figure 49.8.

Figure 49.10 Results of Linear Rank Tests of Treatment

	The LIFETEST Procedure						
Un	ivariate Chi-S	Squares for t	he Wilcoxon Te	st			
	Test	Standard		Pr >			
Variable	Statistic	Error	Chi-Square	Chi-Square			
Treatment	3.9525	1.7524	5.0875	0.0241			
Un	Univariate Chi-Squares for the Log-Rank Test						
	Test	Standard		Pr >			
Variable	Statistic	Error	Chi-Square	Chi-Square			
Treatment	6.2708	2.6793	5.4779	0.0193			

With Sex as a prognostic factor that you want to control, you can compute a stratified linear rank statistic to test the effect of Treatment by specifying Sex in the STRATA statement and Treatment in the TEST statement as in the following program. The TEST=NONE option is specified in the STRATA statement to suppress the two-sample tests for Sex.

```
proc lifetest data=Exposed notable;
  time Days*Status(0);
  strata Sex / test=none;
  test Treatment;
run;
```

Results of the stratified linear rank tests are shown in Figure 49.11. The *p*-values are very similar to those of the stratified tests in Figure 49.9.

Figure 49.11 Results of Stratified Linear Rank Tests of Treatment

The LIFETEST Procedure						
Un	ivariate Chi-S	quares for t	he Wilcoxon Te	st		
	Test	Standard		Pr >		
Variable	Statistic	Error	Chi-Square	Chi-Square		
Treatment	4.2372	1.7371	5.9503	0.0147		
Univariate Chi-Squares for the Log-Rank Test						
	Test	Standard		Pr >		
Variable	Statistic	Error	Chi-Square	Chi-Square		
Treatment	6.8021	2.5419	7.1609	0.0075		

Syntax: LIFETEST Procedure

The following statements are available in PROC LIFETEST:

```
PROC LIFETEST < options > ;
BY variables;
FREQ variable;
ID variables;
STRATA variable < (list) > < ... variable < (list) >> < /options > ;
TEST variables;
TIME variable < *censor(list) > ;
```

The simplest use of PROC LIFETEST is to request the nonparametric estimates of the survivor function for a sample of survival times. In such a case, only the PROC LIFETEST statement and the TIME statement are required. You can use the STRATA statement to divide the data into various strata. A separate survivor function is then estimated for each stratum, and tests of the homogeneity of strata are performed. However, if the GROUP= option is also specified in the STRATA statement, stratified tests are carried out to test the k samples defined by the GROUP= variable while controlling for the effect of the STRATA variables. You can specify covariates in the TEST statement. PROC LIFETEST computes linear rank statistics to test the effects of these covariates on survival.

The PROC LIFETEST statement invokes the procedure. All statements except the TIME statement are optional, and there is no required order for the statements following the PROC LIFETEST statement. The TIME statement is used to specify the variables that define the survival time and censoring indicator. The STRATA statement specifies a variable or set of variables defining the strata for the analysis. The TEST statement specifies a list of numeric covariates to be tested for their association with the response survival time. Each variable is tested individually, and a joint test statistic is also computed. The ID statement provides a list of variables whose values are used to identify observations in the product-limit, Breslow, or Fleming-Harrington estimates. When only the TIME statement appears, no strata are defined and no tests of homogeneity are performed.

PROC LIFETEST Statement

```
PROC LIFETEST < options > ;
```

The PROC LIFETEST statement invokes the procedure. Optionally, this statement identifies an input and an OUTSURV= data set, and specifies the computation details of the survivor function estimation. The options listed in Table 49.1 are available in the PROC LIFETEST statement and are described in alphabetic order. If no options are requested, PROC LIFETEST computes and displays the product-limit estimate of the survivor function; and if an ODS GRAPHICS ON statement is specified, a plot of the estimated survivor function is also displayed.

 Table 49.1
 Options Available in the PROC LIFETEST Statement

Input and Output Data Sets DATA= Specifies the input SAS data set OUTSURV= Names an output data set to contain survival estimates and confidence limits OUTTEST= Names an output data set to contain rank test statistics for association of survival time with covariates
DATA= Specifies the input SAS data set OUTSURV= Names an output data set to contain survival estimates and confidence limits OUTTEST= Names an output data set to contain rank test statistics for association of survival time with covariates
OUTSURV= Names an output data set to contain survival estimates and confidence limits OUTTEST= Names an output data set to contain rank test statistics for association of survival time with covariates
OUTTEST= dence limits Names an output data set to contain rank test statistics for association of survival time with covariates
OUTTEST= Names an output data set to contain rank test statistics for association of survival time with covariates
tion of survival time with covariates
Nonparametric Estimation
INTERVALS= Specifies interval endpoints for life-table estimates
NELSON Adds the Nelson-Aalen estimates
METHOD= Specifies the method to compute survivor function
NINTERVAL= Specifies the number of intervals for life-table estimates
WIDTH= Specifies the width of intervals for life-table estimates
Confidence Limits for Survivorship
ALPHA= Sets the confidence level for interval estimation estimates
BANDMAXTIME= Specifies the maximum time for confidence band
BANDMINTIME= Specifies the minimum time for confidence band
CONFBAND= Specifies the type of confidence band in the OUTSURV= data set
CONFTYPE= Specifies the transformation applied to the survivor function to
obtain confidence limits
Line Printer Plots
FORMCHAR(1,2,7,9)= Defines the characters used for line printer plot axes
LINEPRINTER Specifies that plots be produced by a line printer
MAXTIME= Specifies the maximum time value for plotting
NOCENSPLOT Suppresses the plot of censored observations
PLOTS= Specifies the plots to display
opecines the plots to display
ODS Graphics
MAXTIME= Specifies the maximum time value for plotting
PLOTS= specifies plots to display
Traditional Graphics
ANNOTATE= Specifies an Annotate data set that adds features to plots
CENSOREDSYMBOL= Defines the symbol used for censored observations in plots
DESCRIPTION= specifies the string that appears in the description field of the PROC
GREPLAY master menu for the plots
EVENTSYMBOL= Specifies the symbol used for event observations in plots
GOUT= Specifies the graphics catalog name for saving graphics output
LANNOTATE= Specifies an input data set that contains variables for local annota-
tion
MAXTIME= Specifies the maximum time value for plotting
PLOTS= Specifies the plots to display
Control Output
ATRISK Adds the number of subjects at risk to the survival estimate table
NOPRINT Suppresses the display of printed output

Table 49.1 continued

Option	Description
NOTABLE	Suppresses the display of survival function estimates
INTERVALS=	Displays only the estimate for the smallest time in each interval
NOLEFT	Suppresses the Number Left column in the survival estimate table
TIMELIST=	Specifies a list of time points to display the survival estimate
REDUCEOUT	Specifies that only INTERVAL= or TIMELIST= observations be
	listed in the OUTSURV= data set
Miscellaneous	
ALPHAQT=	Sets the confidence level for survival time quartiles
MISSING	Allows missing values to be a stratum level
SINGULAR=	Sets the tolerance for testing singularity of covariance matrix of rank statistics
STDERR	Outputs the standard error for the survival estimators to the OUT-
	SURV= data set
TIMELIM=	Specifies the time limit used to estimate the mean survival time and
	its standard error

The PLOTS= option in the PROC LIFETEST statement specifies the plots to display. You can select one of the following three types of graphics in PROC LIFETEST: line printer, traditional, and ODS. If you specify the LINEPRINTER option, you get line printer plots; otherwise you get the traditional graphics if ODS Graphics is not enabled, and you get the ODS Graphics plots if the ODS GRAPHICS ON statement is specified. The following table depicts the behavior regarding the type of graphics produced:

ODS Graphics	PROC LIFETEST Options		Behavior
OFF			No graphics
OFF		LINEPRINTER	No graphics
OFF	PLOTS=SURVIVAL		Traditional graphics
OFF	PLOTS=SURVIVAL	LINEPRINTER	Line printer plot
ON			ODS Graphics survival plot
ON		LINEPRINTER	No graphics
ON	PLOTS=SURVIVAL		ODS Graphics
ON	PLOTS=SURVIVAL	LINEPRINTER	Line printer plot

ODS Graphics is now the preferred method of requesting graphics. Many new features have been added to the ODS Graphics plots in PROC LIFETEST. For example, you can display the number of subjects at risk in a survival plot through ODS Graphics, but such a feature is not available in traditional graphics or line printer plots. The PLOTS= option syntax is documented separately for each type of graphics and is preceded by a heading that indicates the graphics type.

$ALPHA=\alpha$

specifies the level of significance α for the $100(1-\alpha)\%$ confidence intervals for the survivor, hazard, and density functions. For example, the option ALPHA=0.05 requests the 95% confidence limits for the survivor function. The default value is 0.05.

ALPHAQT= α

specifies the significance level α for the $100(1-\alpha)\%$ confidence intervals for the quartiles of the survival time. For example, the option ALPHAQT=0.05 requests a 95% confidence interval for the quartiles of the survival time. The default value is 0.05.

ANNOTATE=SAS-data-set

ANNO=SAS-data-set

specifies an input data set that contains appropriate variables for annotation of the traditional graphics. The ANNOTATE= option enables you to add features (for example, labels explaining extreme observations) to plots produced on graphics devices. The ANNOTATE= option cannot be used if the LINEPRINTER option or the ODS GRAPHICS ON statement is specified. The data set specified must be an ANNOTATE= type data set, as described in *SAS/GRAPH Software: Reference*.

The data set specified with the ANNOTATE= option in the PROC LIFETEST statement is "global" in the sense that the information in this data set is displayed in every plot produced by a single invocation of PROC LIFETEST.

ATRISK

adds a column that represents the number of subjects at risk to the survival estimate table. Also added is a column that represents the number of events at each observed time. This option has no effect for the life-table method.

BANDMAXTIME=value

BANDMAX=value

specifies the maximum time for the confidence bands. The default is the largest observed event time. If the specified BANDMAX= time exceeds the largest observed event time, it is truncated to the largest observed event time.

BANDMINTIME=*value*

BANDMIN=value

specifies the minimum time for the confidence bands. The default is the smallest observed event time. For the equal-precision band, if the BANDMIN= value is less than the smallest observed event time, it is defaulted to the smallest observed event time.

CENSOREDSYMBOL=*name* | 'string'

CS=name | 'string'

specifies the symbol value for the censored observations in traditional graphics. The value, *name* or 'string', is the symbol value specification allowed in SAS/GRAPH software. The default is CS=CIRCLE. If you want to omit plotting the censored observations, specify CS=NONE. The CENSOREDSYMBOL= option cannot be used if the LINEPRINTER option or the ODS GRAPHICS ON statement is specified.

CONFBAND=keyword

specifies the confidence bands to be output to the OUTSURV= data set. Confidence bands are available for METHOD=KM, METHOD=BRESLOW, or METHOD=FH. You can use the following *keywords*:

ALL outputs both the Hall-Wellner and the equal-precision confidence bands.

EP outputs the equal-precision confidence bands.

HW outputs the Hall-Wellner confidence bands.

CONFTYPE=*keyword*

specifies the transformation applied to S(t) to obtain the pointwise confidence intervals and the confidence bands for the survivor function as well as the confidence intervals for the quartiles of the survival times. The following *keywords* can be used and the default is CONFTYPE=LOGLOG.

ASINSQRT the arcsine-square root transformation

$$g(x) = \sin^{-1}(\sqrt{x})$$

LOGLOG the log-log transformation

$$g(x) = \log(-\log(x))$$

This is also referred to as the log cumulative hazard transformation since it is applying the logarithmic function log(.) to the cumulative hazard function. Collett (1994) and Lachin (2000) refer it as the complementary log-log transformation.

LINEAR the identity transformation

$$g(x) = x$$

LOG the logarithmic transformation

$$g(x) = \log(x)$$

LOGIT the logit transformation

$$g(x) = \log\left(\frac{x}{1-x}\right)$$

DATA=SAS-data-set

names the SAS data set used by PROC LIFETEST. By default, the most recently created SAS data set is used.

DESCRIPTION='string'

DES='string'

specifies a descriptive string of up to 256 characters that appears in the "Description" field of the traditional graphics catalog. The description does not appear in the plots. By default, PROC LIFETEST assigns a description of the form PLOT OF *vname* vs *hname*, where *vname* and *hname* are the names of the *y* variable and the *x* variable, respectively. The DESCRIPTION= option cannot be used if the LINEPRINTER option or the ODS GRAPHICS ON statement is specified.

EVENTSYMBOL=name | 'string'

ES=name | 'string'

specifies the symbol value for the event observations in traditional graphics. The value, *name* or 'string', is the symbol value specification allowed in SAS/GRAPH software. The default is ES=NONE. The EVENTSYMBOL= option cannot be used if the LINEPRINTER option or the ODS GRAPHICS ON statement is specified.

FORMCHAR(1,2,7,9)='string'

defines the characters used for constructing the vertical and horizontal axes of the line printer plots. The string should be four characters. The first and second characters define the vertical and horizontal bars, respectively, which are also used in drawing the *steps* of the Kaplan-Meier, Breslow, or Fleming-Harrington survival curve. The third character defines the tick mark for the axes, and the fourth character defines the lower left corner of the plot. The default is FORMCHAR(1,2,7,9)='l-+-'. Any character or hexadecimal string can be used to customize the plot appearance. If you use hexadecimals, you must put an x after the closing quote. For example, to send the plot output to a printer with the IBM graphics character set (1 or 2), specify

```
formchar (1, 2, 7, 9) = 'B3C4C5C0'x
```

Refer to the chapter titled "The PLOT Procedure" in the *Base SAS Procedures Guide* for further information.

GOUT=graphics-catalog

specifies the graphics catalog for saving traditional graphics output from PROC LIFETEST. The default is WORK.GSEG. The GOUT= option cannot be used if the LINEPRINTER option or the ODS GRAPHICS ON statement is specified. For more information, refer to the chapter titled "The GREPLAY Procedure" in SAS/GRAPH Software: Reference.

INTERVALS=values

specifies a list of interval endpoints for the life-table method. These endpoints must all be nonnegative numbers. The initial interval is assumed to start at zero whether or not zero is specified in the list. Each interval contains its lower endpoint but does not contain its upper endpoint. When this option is used with METHOD=KM, METHOD=BRESLOW, or METHOD=FH, it reduces the number of survival estimates displayed by showing only the estimates for the smallest time within each specified interval. The INTERVALS= option can be specified in any of the following ways:

list separated by blanks	intervals=1 3 5 7
list separated by commas	intervals=1,3,5,7
x to y	intervals=1 to 7
x to y by z	intervals=1 to 7 by 1
combination of the above	intervals=1,3 to 5,7

For example, the specification

intervals=5,10 to 30 by 10

produces the set of intervals

```
\{[0,5), [5,10), [10,20), [20,30), [30,\infty)\}
```

LANNOTATE=SAS-data-set

LANN=SAS-data-set

specifies an input data set that contains variables for local annotation of traditional graphics. You can use the LANNOTATE= option to specify a different annotation for each BY group, in which case the BY variables must be included in the LANNOTATE= data set. The LANNOTATE= option cannot be used if the LINEPRINTER option or the ODS GRAPHICS ON statement is specified. The data set specified must be an ANNOTATE= type data set, as described in *SAS/GRAPH Software: Reference*.

If there is no BY-group processing, the ANNOTATE= and LANNOTATE= options have the same effects.

LINEPRINTER

LS

specifies that plots are produced by a line printer instead of by a graphical device.

MAXTIME=value

specifies the maximum value of the time variable allowed on the plots so that outlying points do not determine the scale of the time axis of the plots. This option affects only the displayed plots and has no effect on any calculations.

METHOD=type

specifies the method to be used to compute the survival function estimates. Valid values for *type* are as follows:

Breslow

specifies that the Breslow estimates be computed. The Breslow estimator is the exponentiation of the negative Nelson-Aalen estimator of the cumulative hazard function.

FΗ

specifies that the Fleming-Harrington (FH) estimates be computed. The FH estimator is a tie-breaking modification of the Breslow estimator. If there are no tied event times, this estimator is the same as the Breslow estimator.

KM

PL

specifies that Kaplan-Meier estimates (also known as the product-limit estimates) be computed.

ACT

LIFE

LT

specifies that life-table estimates (also known as actuarial estimates) be computed.

By default, METHOD=KM.

MISSING

allows missing values for numeric variables and blank values for character variables as valid stratum levels. See the section "Missing Values" on page 3735 for details.

By default, PROC LIFETEST does not use observations with missing values for any stratum variables.

NELSON

AALEN

produces the Nelson-Aalen estimates of the cumulative hazards and the corresponding standard errors. This option is ignored if METHOD=LT is specified.

NINTERVAL=value

specifies the number of intervals used to compute the life-table estimates of the survivor function. This parameter is overridden by the WIDTH= option or the INTERVALS= option. When you specify the NINTERVAL= option, PROC LIFETEST tries to find an interval that results in round numbers for the endpoints. Consequently, the number of intervals can be different from the number requested. Use the INTERVALS= option to control the interval endpoints. The default is NINTERVAL=10.

NOCENSPLOT

NOCENS

requests that the plot of censored observations be suppressed when the LINEPRINTER and PLOTS= options are specified. This option is not needed when the life-table method is used to compute the survival estimates, since the plot of censored observations is not produced.

NOLEFT

suppress the Number Left column in the survival estimate table. Also suppressed is the Number Event column. This option has no effect for life-table estimate.

NOPRINT

suppresses the display of output. This option is useful when only an output data set is needed. Note that this option temporarily disables the Output Delivery System (ODS); see Chapter 20, "Using the Output Delivery System" for more information.

NOTABLE

suppresses the display of survival function estimates. Only the number of censored and event times, plots, and test results is displayed.

OUTSURV=SAS-data-set

OUTS=SAS-data-set

creates an output SAS data set to contain the estimates of the survival function and corresponding confidence limits for all strata. See the section "OUTSURV= Data Set" on page 3753 for more information about the contents of the OUTSURV= data set.

OUTTEST=SAS-data-set

OUTT=SAS-data-set

creates an output SAS data set to contain the overall chi-square test statistic for association with failure time for the variables in the TEST statement, the values of the univariate rank test

statistics for each variable in the TEST statement, and the estimated covariance matrix of the univariate rank test statistics. See the section "OUTTEST= Data Set" on page 3754 for more information about the contents of the OUTTEST= data set.

Line Printer PLOTS= Option

PLOTS=plot-request

PLOTS=(plot-requests)

controls the line printer plots produced. You must also specify the LINEPRINTER option to obtain line printer plots. When you specify only one plot-request, you can omit the parentheses around the plot-request. Here are some examples:

```
plots=s
plots=(s ls lls)
```

The *plot-requests* include the following:

CENSORED

C

specifies a plot of censored observations. This option is available for METHOD=KM, METHOD=BRESLOW, or METHOD=FH only.

SURVIVAL

S

specifies a plot of the estimated SDF versus time.

LOGSURV

LS

specifies a plot of the $-\log(\text{estimated SDF})$ versus time.

LOGLOGS

LLS

specifies a plot of the log(-log(estimated SDF)) versus log(time).

HAZARD

Н

specifies a plot of the estimated hazard function versus time (life-table method only).

PDF

Р

specifies a plot of the estimated probability density function versus time (life-table method only).

ODS Graphics PLOTS= Option

```
PLOTS< (global-plot-option) > = plot-request < (options) >
```

```
PLOTS< (global-plot-option) > = (plot-request < (options) > < ... plot-request < (options) > >) controls the plots produced using ODS Graphics. When you specify only one plot-request, you can omit the parentheses around the plot-request. Here are some examples:
```

```
plots=none
plots=(survival(atrisk=100 to 350 by 50) logsurv)
plots(only)=hazard
```

You must enable ODS Graphics before requesting plots—for example, like this:

```
ods graphics on;
proc lifetest plots=survival(atrisk);
   time T*Status(0);
run;
ods graphics off;
```

For general information about ODS Graphics, see Chapter 21, "Statistical Graphics Using ODS." If you have enabled ODS Graphics but do not specify the PLOTS= option, then PROC LIFETEST produces a plot of the estimated survivor functions by default. The only global plot option follows:

ONLY

specifies that only the specified plots in the list be produced; otherwise, the default survivor function plot is also displayed.

The *plot-requests* and *plot-request* options include the following.

ALL

produces all appropriate plots. For METHOD=KM, METHOD=BRESLOW, or METHOD=FH, specifying PLOTS=ALL is equivalent to specifying PLOTS=(SURVIVAL LOGSURV LOGLOGLS HAZARD); for the life-table method, PLOTS=ALL is equivalent to specifying PLOTS=(SURVIVAL LOGSURV LOGLOGS DENSITY HAZARD).

HAZARD < (hazard-options) >

H < hazard-options >

plots the estimated hazard functions. Kernel-smoothed estimates are produced for METHOD=KM, METHOD=BRESLOW, or METHOD=FH. You can specify the following *hazard-options*, but only the CL option can be used for the life-table method:

BANDWIDTH=bandwidth-option

BW=bandwidth-option

specifies what bandwidth is chosen for the kernel-smoothing and how it is chosen. You can specify one of the following *bandwidth-options*.

value

sets the bandwidth to the given value.

numeric-list

selects the bandwidth from the given *numeric-list* that minimizes the mean integrated squared error.

RANGE(lower,upper)

selects the bandwidth from the interval (*lower, upper*) that minimizes the mean integrated squared error. PROC LIFETEST uses the golden section search algorithm to find the minimum. If there is more than one local minimum in the interval, there is no guarantee that the local minimum found is also the global minimum.

See the section "Optimal Bandwidth" on page 3746 for details about the mean integrated squared error. If the BANDWIDTH= option is not specified, the default is BANDWIDTH= RANGE(0.2b,20b), where $b=\frac{g_u-g_l}{8n\cdot 2}$, g_l and g_u are the values of the GRIDL= and GRIDU= options, respectively, and n is the total number of noncensored observations.

GRIDL=number

specifies the lower grid limit for the kernel-smoothed estimate. The default value is the time origin.

GRIDU=number

specifies the upper grid limit for the kernel-smoothed estimate. The default value equals the maximum event time

KERNEL=*kernel-option*

specifies the kernel used. The choices are as follows:

BIWEIGHT

BW

$$K_{BW}(x) = \frac{15}{16}(1 - x^2)^2, \qquad -1 \le x \le 1$$

EPANECHNIKOV

Ε

$$K_E(x) = \frac{3}{4}(1 - x^2), \qquad -1 \le x \le 1$$

UNIFORM

U

$$K_U(x) = \frac{1}{2}, \qquad -1 \le x \le 1$$

The default is KERNEL=EPANECHNIKOV.

NMINGRID=number

specifies the number of grid points in determining the mean integrated square error (MISE). The default value is 51.

NGRID=number

specifies the number of grid points. The default is 101.

CL

displays the pointwise confidence limits for the smoothed hazard.

LOGLOGS

LLS

plots the log of negative log of estimated survivor functions versus the log of time.

LOGSURV

LS

plots the negative log of estimated survivor functions versus time.

NONE

suppresses all plots.

PDF < (CL) >

plots the estimated probability density functions (life-table method only). Pointwise confidence limits are displayed optionally by specifying the CL option.

SURVIVAL < (survival-options) >

S < (survival-options) >

plots the estimated survivor functions. Censored times are plotted as a plus sign on the Kaplan-Meier, Breslow, or Fleming-Harrington survival curves unless the NOCENSOR option is specified. You can customize the display by using the following *survival-options*:

ATRISK <= number-list >

displays the numbers of subjects at risk at the given times. The *number-list* identifies the times at which the numbers at risk are displayed. If the *number-list* is not specified, PROC LIFETEST uses the default list $\{0, a, 2a, ..., n \times a\}$, where a and n are computed by the following algorithm. Let m be the MAXTIME= value or the largest observed time if the MAXTIME= option is not specified; let $b = 10^{\text{ceil}[\log_{10}(m)-1]}$, where ceil() is the ceiling function.

$$a = \begin{cases} \frac{b}{2} & \text{if } m < 0.25b \\ 2b & \text{if } m > 0.75b \\ b & \text{otherwise} \end{cases}$$

$$n = \text{integral value of } m/a$$

CB <=keyword>

displays the confidence bands (that is, simultaneous confidence intervals) for the survivor functions. You can specify one of the following *keywords*. The default is CB=HW.

ALL

displays both the equal-precision and the Hall-Wellner bands.

ΕP

displays the equal-precision band.

HW

displays the Hall-Wellner confidence band.

CL

displays the pointwise confidence limits for the survivor functions.

FAILURE

F

changes all the displays for survivor functions to those for the failure functions. For example, if both the FAILURE and CL options are specified, the plot displays the failure curves as well as the pointwise confidence limits for the failure functions.

NOCENSOR

suppresses the plotting of the censored times on a Kaplan-Meier, Breslow, or Fleming-Harrington survival curve.

STRATA=strata-option

specifies how to display the survival/failure curves for multiple strata. This option has no effect if there is only one stratum. You can choose one of the following *strata options*:

INDIVIDUAL

UNPACK

specifies that a separate plot be displayed for each stratum.

OVERLAY

specifies that the survival/failure curves for the strata be overlaid in one plot.

PANEL

specifies that separate plots for the strata be organized into panels of two or four plots, depending on the number of strata.

The default is STRATA=OVERLAY.

TEST

displays the *p*-value of a homogeneity test specified in the STRATA statement. If more than one test is produced, the test is chosen in the following order: LOGRANK, WILCOXON, TARONE, PETO, MODPETO, FLEMING, and LR.

Traditional Graphics PLOTS = Option

```
PLOTS=plot-request < (NAME=name | 'string') >
PLOTS=(plot-request < (NAME=name | 'string') > <, ..., plot-request < (NAME=name | 'string') > >)
```

controls plots produced in traditional graphics. To obtain traditional graphics, you must neither enable ODS Graphics nor specify the LINEPRINTER option. For each *plot-request*, you can use the NAME= option to specify a name to identify the plot. The name can be specified as a SAS name or as a quoted string of up to 256 characters. Only the first eight characters are used as the entry name in the GOUT= catalog. The *plot-requests* include the following:

SURVIVAL

S

plots the estimated survivor functions versus time.

LOGSURV

LS

plots the negative log of estimated survivor functions versus time.

LOGLOGS

LLS

plots the log of negative log of estimated survivor functions versus the log of time.

HAZARD

Н

plots estimated hazard function versus time (life-table method only).

PDF

Р

plots the estimated probability density function versus time (life-table method only).

When you specify only one *plot-request*, you can omit the parentheses around the *plot-request*. Here are some examples:

```
plots=s
plots=(s(name=Surv2), h(name=Haz2))
```

The latter requests a plot of the estimated survivor function versus time and a plot of the estimated hazard function versus time, with Surv2 and Haz2 as their names in the GOUT= catalog, respectively.

REDUCEOUT

specifies that the OUTSURV= data set contain only those observations that are included in the INTERVALS= or TIMELIST= option. This option has no effect if the OUTSURV= option is not specified. It also has no effect if neither the INTERVALS= option nor the TIMELIST= option is specified.

SINGULAR=value

specifies the tolerance for testing singularity of the covariance matrix for the rank test statistics. The test requires that a pivot for sweeping a covariance matrix be at least this number times a norm of the matrix. The default value is 1E–12.

STDERR

specifies that the standard error of the survivor function (SDF_STDERR) be output to the OUTSURV= data set. If the life-table method is used, the standard error of the density function (PDF_STDERR) and the standard error of the hazard function (HAZ_STDERR) are also output.

TIMELIM=time-limit

specifies the time limit used in the estimation of the mean survival time and its standard error. The mean survival time can be shown to be the area under the Kaplan-Meier survival curve. However, if the largest observed time in the data is censored, the area under the survival curve is not a closed area. In such a situation, you can choose a time limit L and estimate the mean survival curve limited to a time L (Lee 1992, pp. 72–76). This option is ignored if the largest observed time is an event time. Valid *time-limit* values are as follows:

EVENT

LET

specifies that the time limit L be the largest event time in the data. TIMELIM=EVENT is the default.

OBSERVED

LOT

specifies that the time limit L be the largest observed time in the data.

number

specifies that the time limit L be the given *number*. The *number* must be positive and at least as large as the largest event time in the data.

TIMELIST=number-list

specifies a list of time points at which the Kaplan-Meier estimates are displayed. The time points are listed in the column labeled Timelist. Since the Kaplan-Meier survival curve is a decreasing step function, each given time point falls in an interval that has a constant survival estimate. The event time that corresponds to the beginning of the time interval is displayed along with its survival estimate.

WIDTH=value

sets the width of the intervals used in the life-table calculation of the survival function. This parameter is overridden by the INTERVALS= option.

BY Statement

BY variables;

You can specify a BY statement with PROC LIFETEST to obtain separate analyses on observations in groups that are defined by the BY variables. When a BY statement appears, the procedure expects the input data set to be sorted in order of the BY variables. If you specify more than one BY statement, only the last one specified is used.

If your input data set is not sorted in ascending order, use one of the following alternatives:

- Sort the data by using the SORT procedure with a similar BY statement.
- Specify the NOTSORTED or DESCENDING option in the BY statement for the LIFETEST procedure. The NOTSORTED option does not mean that the data are unsorted but rather that

the data are arranged in groups (according to values of the BY variables) and that these groups are not necessarily in alphabetical or increasing numeric order.

• Create an index on the BY variables by using the DATASETS procedure (in Base SAS software).

The BY statement is more efficient than the STRATA statement for defining strata in large data sets. However, if you use the BY statement to define strata, PROC LIFETEST does not pool over strata for testing the association of survival time with covariates, nor does it test for homogeneity across the BY groups.

When the life-table method is used to estimate survivor functions, each BY group might have a different set of intervals. To make intervals the same across BY groups, use the INTERVALS= or WIDTH= option in the PROC LIFETEST statement.

For more information about BY-group processing, see the discussion in *SAS Language Reference: Concepts.* For more information about the DATASETS procedure, see the discussion in the *Base SAS Procedures Guide.*

FREQ Statement

FREQ variable < /option > ;

The FREQ statement identifies a *variable* that contains the frequency of occurrence of each observation. PROC LIFETEST treats each observation as if it appeared *n* times, where *n* is the value of the FREQ variable for the observation. The FREQ statement is useful for producing life tables when the data are already in the form of a summary data set. If it is not an integer, it is truncated to an integer unless the NOTRUNCATE option is specified. If it is missing or less than or equal zero, the observation is not used.

The following option can be specified in the FREQ statement after a slash (/):

NOTRUNCATE

NOTRUNC

specifies that the frequency values are not truncated to integers. This option does not apply to the Fleming-Harrington estimator (METHOD=FH).

ID Statement

ID variables;

The ID statement identifies *variables* whose values are used to label the observations of the Kaplan-Meier, Breslow, or Fleming-Harrington survivor function estimates. SAS format statements can be used to format the values of the ID variables.

STRATA Statement

```
STRATA variable < (list) > < . . . variable < (list) > > </options > ;
```

The STRATA statement identifies the variables that determine the strata levels. Strata are formed according to the nonmissing values of these variables. The MISSING option can be used to allow missing values as a valid stratum level. Other options enable you to specify various *k*-sample tests, stratified tests, or trend tests and to make multiple-comparison adjustments for paired differences.

In the preceding syntax, *variable* is a variable whose values determine the stratum levels, and *list* is a list of endpoints for a numeric variable. The values for *variable* can be formatted or unformatted. If the variable is a character variable, or if the variable is numeric and no list appears, then the strata are defined by the unique values of the strata variable. More than one variable can be specified in the STRATA statement, and each numeric variable can be followed by a list. Each interval contains its lower endpoint but not its upper endpoint. The corresponding strata are formed by the combination of levels. If a variable is numeric and is followed by a list, then the levels for that variable correspond to the intervals defined by the list. The initial interval is assumed to start at $-\infty$, and the final interval is assumed to end at ∞ .

The specification of STRATA variables can have any of the following forms:

```
list separated by blanks
strata age (5 10 20 30)

list separated by commas
x \text{ to } y
strata age (5, 10, 20, 30)

x \text{ to } y \text{ strata age (5 to 10)}

x \text{ to } y \text{ by } z
strata age (5 to 30 by 10)

combination of the above
strata age (5, 10 to 50 by 10)
```

For example, the specification

```
strata Age (5,20 to 50 by 10) Sex;
```

indicates the following levels for the Age variable:

```
\{(-\infty, 5), [5, 20), [20, 30), [30, 40), [40, 50), [50, \infty)\}
```

This statement also specifies that the Age strata be further subdivided by values of the variable Sex. In this example, there are 6 age groups by 2 sex groups, forming a total of 12 strata.

The specification of several strata variables, such as

```
strata A B C;
```

is equivalent to the A*B*C syntax of the TABLES statement in the FREQ procedure. The number of strata levels usually grows very rapidly with the number of STRATA variables, so you must be cautious when specifying the list of STRATA variables.

When comparing more than two survival curves, a *k*-sample test tells you whether the curves are significantly different from each other, but it does not identify which pairs of curves are different. A multiple-comparison adjustment of the *p*-values for the paired comparisons retains the same overall false positives as the *k*-sample test. Two types of paired comparisons can be made: comparisons between all pairs of curves and comparisons between a control curve and all other curves. You use the DIFF= option to specify the comparison type, and you use the ADJUST= option to select a method of multiple-comparison adjustments.

Table 49.2 summaries the options available in the STRATA statement.

 Table 49.2
 Options Available in the STRATA Statement

Option	Description
Homogeneity Tests	
GROUP=	Specifies the group variable for stratified tests
NODETAIL	Suppresses printing the test statistic and covariance matrix
NOTEST	Suppresses any tests
TEST=	Specifies tests corresponding to various weight functions
TREND	Requests a trend test
Multiple Comparisons	
ADJUST=	Requests a multiple-comparison adjustment
DIFF=	Specifies the type of differences to consider
Missing Strata Value	
MISSING	Allows missing values as valid stratum values

Options in the STRATA statement are specified after a slash ("/"). The following list describes these options.

ADJUST=method

specifies the multiple-comparison method for adjusting the p-values of the paired tests. See the section "Multiple-Comparison Adjustments" on page 3748 for mathematical details; also see Westfall et al. (1999). The adjustment methods include the following:

BONFERRONI

BON

applies the Bonferroni correction to the raw p-values.

DUNNETT

performs Dunnett's two-tailed comparisons of the control group with all other groups. PROC LIFETEST uses the factor-analytic covariance approximation described in Hsu (1992) and identifies the adjustment in the results as "Dunnett-Hsu." Note that ADJUST=DUNNETT is incompatible with DIFF=ALL.

SCHEFFE

performs Scheffé's multiple-comparison adjustment.

SIDAK

applies the Šidák correction to the raw p-values.

SMM

GTE

performs the paired comparisons based on the studentized maximum modulus test.

TUKEY

performs the paired comparisons based on Tukey's studentized range test. PROC LIFETEST uses the approximation described in Kramer (1956) and identifies the adjustment as "Tukey-Kramer" in the results. Note that ADJUST=TUKEY is incompatible with DIFF=CONTROL.

SIMULATE < (simulate-options) >

computes the adjusted p-values from the simulated distribution of the maximum or maximum absolute value of a multivariate normal random vector. The simulation estimates q, the true $(1 - \alpha)$ th quantile, where α is the value of the ALPHA= *simulate-option*.

The number of samples for the SIMULATE adjustment is set so that the tail area for the simulated q is within a certain accuracy radius γ of $1 - \alpha$ with an accuracy confidence of $100(1 - \epsilon)\%$. In equation form,

$$\Pr(|F(\hat{q}) - (1 - \alpha)| \le \gamma) = 1 - \epsilon$$

where \hat{q} is the simulated q and F is the true distribution function of the maximum; see Edwards and Berry (1987) for details. By default, $\gamma = 0.005$ and $\epsilon = 0.01$ so that the tail area of \hat{q} is within 0.005 of 0.95 with 99% confidence.

The *simulate-options* include the following:

ACC=value

specifies the target accuracy radius γ of a $100(1-\epsilon)\%$ confidence interval for the true probability content of the estimated $(1-\alpha)$ th quantile. The default value is ACC=0.005.

ALPHA=value

specifies the value α for estimating the $(1 - \alpha)$ th quantile. The default value is the ALPHA= value in the PROC LIFETEST statement, or 0.05 if that option is not specified.

EPS=value

specifies the value ϵ for a $100(1-\epsilon)\%$ confidence interval for the true probability content of the estimated $(1-\alpha)$ th quantile. The default value for the accuracy confidence is 99%, corresponding to EPS=0.01.

NSAMP=n

specifies the sample size for the simulation. By default, n is set based on the

values of the target accuracy radius γ and accuracy confidence $100(1-\epsilon)\%$ for an interval for the true probability content of the estimated $(1-\alpha)$ th quantile. With the default values for γ , ϵ , and α (0.005, 0.01, and 0.05, respectively), NSAMP=12604 by default.

REPORT

specifies that a report on the simulation should be displayed, including a listing of the parameters, such as γ , ϵ , and α , as well as an analysis of various methods for estimating or approximating the quantile.

SEED=number

specifies an integer used to start the pseudo-random number generator for the simulation. If you do not specify a seed, or if you specify a value less than or equal to zero, the seed is by default generated from reading the time of day from the computer's clock.

DIFF=ALL | CONTROL<('string'<..., 'string'>)>

specifies which pairs of survival curves are considered for the multiple comparisons.

DIFF=ALL

requests all paired comparisons

DIFF=CONTROL < ('string' < . . . 'string' >) >

requests comparisons of the control curve with all other curves. To specify the control curve, you specify the quotes strings of formatted values that represent the curve in parentheses. For example, if Cell='large' identifies the control group, you specify

```
DIFF=CONTROL('large')
```

If more than one variable is used to identify the curves (for example, if Cell='large' and Sex='F' represent the control), you specify

```
DIFF=CONTROL('large' 'F')
```

The order of the quoted strings should correspond to the order of the stratum variables. If no specific curve is specified as the control, the first stratum or group value is used.

By default, DIFF=ALL unless you specify ADJUST=DUNNETT, in which case DIFF=CONTROL.

GROUP=variable

specifies the variable whose formatted values identify the various samples whose underlying survival curves are to be compared. The tests are stratified on the levels of the STRATA variables. For instance, in a multicenter trial in which two forms of therapy are to be compared, you specify the variable identifying therapies as the GROUP= variable and the variable identifying centers as the STRATA variable, in order to perform a stratified test to compare the therapies while controlling the effect of the centers.

MISSING

allows missing values to be a stratum level or a valid value of the GROUP= variable.

NODETAIL

suppresses the display of the rank statistics and the corresponding covariance matrices for various strata. If the TREND option is specified, the display of the scores for computing the trend tests is suppressed.

NOTEST

suppresses the *k*-sample tests, stratified tests, and trend tests.

TREND

computes the trend tests for testing the null hypothesis that the k population hazards rate are the same versus an ordered alternatives. If there is only one STRATA variable and the variable is numeric, the unformatted values of the variable are used as the scores; otherwise, the scores are $1, 2, \ldots$, in the given order of the strata.

TEST=test-request

TEST=(test-request < . . . test-request >)

controls the tests produced. Each test corresponds to a different weight function (see the section "Nonparametric Tests" on page 3747 for the weight functions). The test requests include the following:

ALL Specifies all the nonparametric tests with $\rho 1=1$ and $\rho 2=0$ for the Fleming

and Harrington test—FLEMING(1,0).

FLEMING($\rho 1, \rho 2$) Specifies the family of tests in Harrington and Fleming (1982), where

 $\rho 1$ and $\rho 2$ are nonnegative numbers. FLEMING($\rho 1, \rho 2$) reduces to the Fleming-Harrington G^{ρ} family (Fleming and Harrington 1981) when $\rho 2$ =0, which you can specify as FLEMING(ρ) with one argument. When ρ =0, the test becomes the log-rank test. When ρ =1, the test

should be very close to the Peto-Peto test.

LOGRANK Specifies the log-rank test.

NONE Suppresses all comparison tests. Specifying TEST=NONE is equivalent

to specify NOTEST.

LR Specifies the likelihood ratio test based on the exponential model.

MODPETO Specifies the modified Peto-Peto test.

PETO Specifies the Peto-Peto test. The test is also referred to as the Peto-Peto-

Prentice test.

WILCOXON Specifies the Wilcoxon test. The test is also referred to as the Gehan

test or the Breslow test.

TARONE Specifies the Tarone-Ware test.

By default, TEST=(LOGRANK WILCOXON LR) for the *k*-sample tests, and TEST=(LOGRANK WILCOXON) for stratified and trend tests.

TEST Statement

TEST variables;

The TEST statement specifies a list of numeric covariates (prognostic variables) that you want tested for association with the failure time.

Two sets of rank statistics are computed. These rank statistics and their variances are pooled over all strata. Univariate (marginal) test statistics are displayed for each of the covariates.

Additionally, a sequence of test statistics for joint effects of covariates is displayed. The first element of the sequence is the largest univariate test statistic. Other variables are then added on the basis of the largest increase in the joint test statistic. The process continues until all the variables have been added or until the remaining variables are linearly dependent on the previously added variables.

See the section "Rank Tests for the Association of Survival Time with Covariates" on page 3750 for more information.

TIME Statement

```
TIME variable < *censor(list) > ;
```

The TIME statement is required. It is used to indicate the failure time variable, where *variable* is the name of the failure time variable that can be optionally followed by an asterisk, the name of the censoring variable, and a parenthetical list of values that correspond to right censoring. The censoring values should be numeric, nonmissing values. For example, the statement

```
time T*Flag(1,2);
```

identifies the variable T as containing the observed failure times (event or censored). If the variable Flag has the value 1 or 2, the corresponding value of T is a right-censored value.

Details: LIFETEST Procedure

Missing Values

Observations with a missing value for either the failure time or the censoring variable are not used in the analysis. If a stratum variable value is missing, the observation is not used; however, the MISSING option can be used to request that missing values be treated as valid stratum values. If any variable specified in the TEST statement has a missing value, that observation is not used in the calculation of the rank statistics.

Computational Formulas

Breslow, Fleming-Harrington, and Kaplan-Meier Methods

Let $t_1 < t_2 < \cdots < t_D$ represent the distinct event times. For each $i = 1, \dots, D$, let n_i be the number of surviving units (the size of the risk set) just prior to t_i . Let d_i be the number of units that fail at t_i , and let $s_i = n_i - d_i$. If the NOTRUNCATE option is specified in the FREQ statement, n_i , d_i , and s_i can be nonintegers.

The Breslow estimate of the survivor function is

$$\hat{S}(t_i) = \exp\left(-\sum_{j=1}^i \frac{d_j}{n_j}\right)$$

Note that the Breslow estimate is the exponentiation of the negative Nelson-Aalen estimate of the cumulative hazard function.

The Fleming-Harrington estimate (Fleming and Harrington 1984) of the survivor function is

$$\hat{S}(t_i) = \exp\left(-\sum_{k=1}^{i} \sum_{j=0}^{d_k-1} \frac{1}{n_k - j}\right)$$

If the frequency values are not integers, the Fleming-Harrington estimate cannot be computed.

The Kaplan-Meier (product-limit) estimate of the survivor function at t_i is the cumulative product

$$\hat{S}(t_i) = \prod_{i=1}^{i} \left(1 - \frac{d_j}{n_j} \right)$$

Notice that all the estimators are defined to be right continuous; that is, the events at t_i are included in the estimate of $S(t_i)$. The corresponding estimate of the standard error is computed using Greenwood's formula (Kalbfleisch and Prentice 1980) as

$$\hat{\sigma}\left(\hat{S}(t_i)\right) = \hat{S}(t_i) \sqrt{\sum_{j=1}^{i} \frac{d_j}{n_j s_j}}$$

The first quartile (or the 25th percentile) of the survival time is the time beyond which 75% of the subjects in the population under study are expected to survive. It is estimated by

$$q_{.25} = \min\{t_j | \hat{S}(t_j) < 0.75\}$$

If $\hat{S}(t)$ is exactly equal to 0.75 from t_j to t_{j+1} , the first quartile is taken to be $(t_j + t_{j+1})/2$. If it happens that $\hat{S}(t)$ is greater than 0.75 for all values of t, the first quartile cannot be estimated and is represented by a missing value in the printed output.

The general formula for estimating the 100pth percentile point is

$$q_p = \min\{t_j | \hat{S}(t_j) < 1 - p\}$$

The second quartile (the median) and the third quartile of survival times correspond to p=0.5 and p=0.75, respectively.

Brookmeyer and Crowley (1982) have constructed the confidence interval for the median survival time based on the confidence interval for the S(t). The methodology is generalized to construct the confidence interval for the 100pth percentile based on a g-transformed confidence interval for S(t) (Klein and Moeschberger 1997). You can use the CONFTYPE= option to specify the g-transformation. The $100(1-\alpha)\%$ confidence interval for the first quantile survival time is the set of all points t that satisfy

$$\left| \frac{g(\hat{S}(t)) - g(1 - 0.25)}{g'(\hat{S}(t))\hat{\sigma}(\hat{S}(t))} \right| \le z_{1 - \frac{\alpha}{2}}$$

where g'(x) is the first derivative of g(x) and $z_{1-\frac{\alpha}{2}}$ is the $100(1-\frac{\alpha}{2})$ th percentile of the standard normal distribution.

Consider the bone marrow transplant data described in Example 49.2. The following table illustrates the construction of the confidence limits for the first quartile in the ALL group. Values of $\frac{g(\hat{S}(t)) - g(1 - 0.25)}{g'(\hat{S}(t))\hat{\sigma}(\hat{S}(t))}$ that lie between $\pm z_{1 - \frac{0.05}{2}} = \pm 1.965$ are highlighted.

Constructing 95% Confidence Limits for the 25th Percentile									
					$\hat{S}(t)$)- $g(1-t)$				
t	$\hat{S}(t)$	$\hat{\sigma}(\hat{S}(t))$	LINEAR	LOGLOG	$g'(\hat{S}(t))\hat{\sigma}(\hat{S}(t))$	ASINSQRT	LOGIT		
1	0.97368	0.025967	8.6141	2.37831	9.7871	4.44648	2.47903		
55	0.94737	0.036224	5.4486	2.36375	6.1098	3.60151	2.46635		
74	0.92105	0.043744	3.9103	2.16833	4.3257	2.94398	2.25757		
86	0.89474	0.049784	2.9073	1.89961	3.1713	2.38164	1.97023		
104	0.86842	0.054836	2.1595	1.59196	2.3217	1.87884	1.64297		
107	0.84211	0.059153	1.5571	1.26050	1.6490	1.41733	1.29331		
109	0.81579	0.062886	1.0462	0.91307	1.0908	0.98624	0.93069		
110	0.78947	0.066135	0.5969	0.55415	0.6123	0.57846	0.56079		
122	0.73684	0.071434	-0.1842	-0.18808	-0.1826	-0.18573	-0.18728		
129	0.71053	0.073570	-0.5365	-0.56842	-0.5222	-0.54859	-0.56101		
172	0.68421	0.075405	-0.8725	-0.95372	-0.8330	-0.90178	-0.93247		
192	0.65789	0.076960	-1.1968	-1.34341	-1.1201	-1.24712	-1.30048		
194	0.63158	0.078252	-1.5133	-1.73709	-1.3870	-1.58613	-1.66406		
230	0.60412	0.079522	-1.8345	-2.14672	-1.6432	-1.92995	-2.03291		
276	0.57666	0.080509	-2.1531	-2.55898	-1.8825	-2.26871	-2.39408		
332	0.54920	0.081223	-2.4722	-2.97389	-2.1070	-2.60380	-2.74691		
383	0.52174	0.081672	-2.7948	-3.39146	-2.3183	-2.93646	-3.09068		
418	0.49428	0.081860	-3.1239	-3.81166	-2.5177	-3.26782	-3.42460		
466	0.46682	0.081788	-3.4624	-4.23445	-2.7062	-3.59898	-3.74781		
487	0.43936	0.081457	-3.8136	-4.65971	-2.8844	-3.93103	-4.05931		
526	0.41190	0.080862	-4.1812	-5.08726	-3.0527	-4.26507	-4.35795		
609	0.38248	0.080260	-4.5791	-5.52446	-3.2091	-4.60719	-4.64271		
662	0.35306	0.079296	-5.0059	-5.96222	-3.3546	-4.95358	-4.90900		

Consider the LINEAR transformation where g(x) = x. The event times that satisfy

 $\left| \frac{g(\hat{S}(t)) - g(1-p)}{g'(\hat{S}(t))\sqrt{\hat{V}(\hat{S}(t))}} \right| \le 1.9599$ include 107, 109, 110, 122, 129, 172, 192, 194, and 230. The confidence of the interval [107, 230] is less than 95%. Brookmeyer and Crowley (1982) suggest extending the confidence interval to but not including the next event time. As such the 95% confidence interval for the first quartile based on the linear transform is [107, 276). The following table lists the confidence intervals for the various transforms.

95% CI's for	the 25th P	ercentile
CONFTYPE	[Lower	Upper)
LINEAR	107	276
LOGLOG	86	230
LOG	107	332
ASINSQRT	104	276
LOGIT	104	230

Sometimes, the confidence limits for the quartiles cannot be estimated. For convenience of explanation, consider the linear transform g(x) = x. If the curve representing the upper confidence limits for the survivor function lies above 0.75, the upper confidence limit for first quartile cannot be estimated. On the other hand, if the curve representing the lower confidence limits for the survivor function lies above 0.75, the lower confidence limit for the quartile cannot be estimated.

The estimated mean survival time is

$$\hat{\mu} = \sum_{i=1}^{D} \hat{S}(t_{i-1})(t_i - t_{i-1})$$

where t_0 is defined to be zero. When the largest observed time is censored, this sum underestimates the mean. The standard error of $\hat{\mu}$ is estimated as

$$\hat{\sigma}(\hat{\mu}) = \sqrt{\frac{m}{m-1} \sum_{i=1}^{D-1} \frac{A_i^2}{n_i s_i}}$$

where

$$A_i = \sum_{j=i}^{D-1} \hat{S}(t_j)(t_{j+1} - t_j)$$

$$m = \sum_{j=1}^{D} d_j$$

If the largest observed time is not an event, you can use the TIMELIM= option to specify a time limit L and estimate the mean survival time limited to the time L and its standard error by replacing k by k+1 with $t_{k+1}=L$.

Nelson-Aalen Estimate of the Cumulative Hazard Function

The Nelson-Aalen cumulative hazard estimator, defined up to the largest observed time on study, is

$$\tilde{H}(t) = \sum_{t_i \le t} \frac{d_i}{n_i}$$

and its estimated variance is

$$\hat{V}(\tilde{H}(t)) = \sum_{t_i \le t} \frac{d_i}{n_i^2}$$

Life-Table Method

The life-table estimates are computed by counting the numbers of censored and uncensored observations that fall into each of the time intervals $[t_{i-1}, t_i)$, i = 1, 2, ..., k+1, where $t_0 = 0$ and $t_{k+1} = \infty$. Let n_i be the number of units entering the interval $[t_{i-1}, t_i)$, and let d_i be the number of events occurring in the interval. Let $b_i = t_i - t_{i-1}$, and let $n'_i = n_i - w_i/2$, where w_i is the number of units censored in the interval. The *effective sample size* of the interval $[t_{i-1}, t_i)$ is denoted by n'_i . Let t_{mi} denote the midpoint of $[t_{i-1}, t_i)$.

The conditional probability of an event in $[t_{i-1}, t_i)$ is estimated by

$$\hat{q}_i = \frac{d_i}{n_i'}$$

and its estimated standard error is

$$\hat{\sigma}\left(\hat{q}_{i}\right) = \sqrt{\frac{\hat{q}_{i}\,\hat{p}_{i}}{n'_{i}}}$$

where $\hat{p}_i = 1 - \hat{q}_i$.

The estimate of the survival function at t_i is

$$\hat{S}(t_i) = \begin{cases} 1 & i = 0\\ \hat{S}(t_{i-1})p_{i-1} & i > 0 \end{cases}$$

and its estimated standard error is

$$\hat{\sigma}\left(\hat{S}(t_i)\right) = \hat{S}(t_i) \sqrt{\sum_{j=1}^{i-1} \frac{\hat{q}_j}{n'_j \hat{p}_j}}$$

The density function at t_{mi} is estimated by

$$\hat{f}(t_{mi}) = \frac{\hat{S}(t_i)\hat{q}_i}{b_i}$$

and its estimated standard error is

$$\hat{\sigma}\left(\hat{f}(t_{mi})\right) = \hat{f}(t_{mi}) \sqrt{\sum_{j=1}^{i-1} \frac{\hat{q}_j}{n'_j \hat{p}_j} + \frac{\hat{p}_i}{n'_i \hat{q}_i}}$$

The estimated hazard function at t_{mi} is

$$\hat{h}(t_{mi}) = \frac{2\hat{q}_i}{b_i(1+\hat{p}_i)}$$

and its estimated standard error is

$$\hat{\sigma}\left(\hat{h}(t_{mi})\right) = \hat{h}(t_{mi})\sqrt{\frac{1 - (b_i\hat{h}(t_{mi})/2)^2}{n_i'\hat{q}_i}}$$

Let $[t_{j-1}, t_j)$ be the interval in which $\hat{S}(t_{j-1}) \geq \hat{S}(t_i)/2 > \hat{S}(t_j)$. The median residual lifetime at t_i is estimated by

$$\hat{M}_i = t_{j-1} - t_i + b_j \frac{\hat{S}(t_{j-1}) - \hat{S}(t_i)/2}{\hat{S}(t_{j-1}) - \hat{S}(t_j)}$$

and the corresponding standard error is estimated by

$$\hat{\sigma}(\hat{M}_i) = \frac{\hat{S}(t_i)}{2\hat{f}(t_{mj})\sqrt{n_i'}}$$

Interval Determination

If you want to determine the intervals exactly, use the INTERVALS= option in the PROC LIFETEST statement to specify the interval endpoints. Use the WIDTH= option to specify the width of the intervals, thus indirectly determining the number of intervals. If neither the INTERVALS= option nor the WIDTH= option is specified in the life-table estimation, the number of intervals is determined by the NINTERVAL= option. The width of the time intervals is 2, 5, or 10 times an integer (possibly a negative integer) power of 10. Let $c = \log_{10}(\text{maximum observed time/number of intervals})$, and let b be the largest integer not exceeding c. Let $d = 10^{c-b}$ and let

$$a = 2 \times I(d \le 2) + 5 \times I(2 < d \le 5) + 10 \times I(d > 5)$$

with I being the indicator function. The width is then given by

width =
$$a \times 10^b$$

By default, NINTERVAL=10.

Pointwise Confidence Limits in the OUTSURV= Data Set

Pointwise confidence limits are computed for the survivor function, and for the density function and hazard function when the life-table method is used. Let α be specified by the ALPHA= option. Let $z_{\alpha/2}$ be the critical value for the standard normal distribution. That is, $\Phi(-z_{\alpha/2}) = \alpha/2$, where Φ is the cumulative distribution function of the standard normal random variable.

Survivor Function

When the computation of confidence limits for the survivor function S(t) is based on the asymptotic normality of the survival estimator $\hat{S}(t)$, the approximate confidence interval might include impossible values outside the range [0,1] at extreme values of t. This problem can be avoided by applying the asymptotic normality to a transformation of S(t) for which the range is unrestricted. In addition, certain transformed confidence intervals for S(t) perform better than the usual linear confidence intervals (Borgan and Liestøl 1990). The CONFTYPE= option enables you to pick one of the following transformations: the log-log function (Kalbfleisch and Prentice 1980), the arcsine-square root function (Nair 1984), the logit function (Meeker and Escobar 1998), the log function, and the linear function.

Let g be the transformation that is being applied to the survivor function S(t). By the delta method, the standard error of $g(\hat{S}(t))$ is estimated by

$$\tau(t) = \hat{\sigma}\left[g(\hat{S}(t))\right] = g'\left(\hat{S}(t)\right)\hat{\sigma}[\hat{S}(t)]$$

where g' is the first derivative of the function g. The $100(1-\alpha)\%$ confidence interval for S(t) is given by

$$g^{-1}\left\{g[\hat{S}(t)] \pm z_{\frac{\alpha}{2}}g'[\hat{S}(t)]\hat{\sigma}[\hat{S}(t)]\right\}$$

where g^{-1} is the inverse function of g.

Arcsine-Square Root Transformation The estimated variance of $\sin^{-1}\left(\sqrt{\hat{S}(t)}\right)$ is $\hat{\tau}^2(t) = \frac{\hat{\sigma}^2[\hat{S}(t)]}{4\hat{S}(t)[1-\hat{S}(t)]}$. The $100(1-\alpha)\%$ confidence interval for S(t) is given by

$$\sin^2\left\{\max\left[0,\sin^{-1}(\sqrt{\hat{S}(t)})-z_{\frac{\alpha}{2}}\hat{\tau}(t)\right]\right\} \leq S(t) \leq \sin^2\left\{\min\left[\frac{\pi}{2},\sin^{-1}(\sqrt{\hat{S}(t)})+z_{\frac{\alpha}{2}}\hat{\tau}(t)\right]\right\}$$

Linear Transformation This is the same as having no transformation in which g is the identity. The $100(1-\alpha)\%$ confidence interval for S(t) is given by

$$\hat{S}(t) - z_{\frac{\alpha}{2}}\hat{\sigma}\left[\hat{S}(t)\right] \le S(t) \le \hat{S}(t) + z_{\frac{\alpha}{2}}\hat{\sigma}\left[\hat{S}(t)\right]$$

Log Transformation The estimated variance of $\log(\hat{S}(t))$ is $\hat{\tau}^2(t) = \frac{\hat{\sigma}^2(\hat{S}(t))}{\hat{S}^2(t)}$. The $100(1-\alpha)\%$ confidence interval for S(t) is given by

$$\hat{S}(t) \exp\left(-z_{\frac{\alpha}{2}}\hat{\tau}(t)\right) \le S(t) \le \hat{S}(t) \exp\left(z_{\frac{\alpha}{2}}\hat{\tau}(t)\right)$$

Log-Log Transformation The estimated variance of $\log(-\log(\hat{S}(t)))$ is $\hat{\tau}^2(t) = \frac{\hat{\sigma}^2[\hat{S}(t)]}{[\hat{S}(t)\log(\hat{S}(t))]^2}$. The $100(1-\alpha)\%$ confidence interval for S(t) is given by

$$\left[\hat{S}(t)\right]^{\exp\left(z_{\frac{\alpha}{2}}\hat{\tau}(t)\right)} \leq S(t) \leq \left[\hat{S}(t)\right]^{\exp\left(-z_{\frac{\alpha}{2}}\hat{\tau}(t)\right)}$$

Logit Transformation The estimated variance of $\log\left(\frac{\hat{S}(t)}{1-\hat{S}(t)}\right)$ is $\hat{\tau}^2(t) = \frac{\hat{\sigma}^2(\hat{S}(t))}{\hat{S}^2(t)[1-\hat{S}(t)]^2}$. The $100(1-\alpha)\%$ confidence limits for S(t) are given by

$$\frac{\hat{S}(t)}{\hat{S}(t) + \left[1 - \hat{S}(t)\right] \exp\left(z_{\frac{\alpha}{2}}\hat{\tau}(t)\right)} \le S(t) \le \frac{\hat{S}(t)}{\hat{S}(t) + \left[1 - \hat{S}(t)\right] \exp\left(-z_{\frac{\alpha}{2}}\hat{\tau}(t)\right)}$$

Density and Hazard Functions

For the life-table method, a $100(1-\alpha)\%$ confidence interval for hazard function or density function at time t is computed as

$$\hat{g}(t) \pm z_{\alpha/2} \hat{\sigma}[\hat{g}(t)]$$

where $\hat{g}(t)$ is the estimate of either the hazard function or the density function at time t, and $\hat{\sigma}[\hat{g}(t)]$ is the corresponding standard error estimate.

Simultaneous Confidence Intervals for Kaplan-Meier Curves

The pointwise confidence interval for the survivor function S(t) is valid for a single fixed time at which the inference is to be made. In some applications, it is of interest to find the upper and lower confidence bands that guarantee, with a given confidence level, that the survivor function falls within the band for all t in some interval. Hall and Wellner (1980) and Nair (1984) provide two different approaches for deriving the confidence bands. An excellent review can be found in Klein and Moeschberger (1997). You can use the CONFBAND= option in the SURVIVAL statement to select the confidence bands. The EP confidence band provides confidence bounds that are proportional to the pointwise confidence interval, while those of the HW band are not proportional to the pointwise confidence bounds. The maximum time, t_{U} , for the bands can be specified by the BANDMAX= option; the minimum time, t_L , can be specified by the BANDMIN= option. Transformations that are used to improve the pointwise confidence intervals can be applied to improve the confidence bands. It might turn out that the upper and lower bounds of the confidence bands are not decreasing in $t_L < t < t_U$, which is contrary to the nonincreasing characteristic of survivor function. Meeker and Escobar (1998) suggest making an adjustment so that the bounds do not increase: if the upper bound is increasing on the right, it is made flat from the minimum to t_{U} ; if the lower bound is increasing from the right, it is made flat from t_L to the maximum. PROC LIFETEST does not make any adjustment for the nondecreasing behavior of the confidence bands in the OUTSURV= data set. However, the adjustment was made in the display of the confidence bands by using ODS Graphics.

For Kaplan-Meier estimation, let $t_1 < t_2 < \ldots < t_D$ be the D distinct events times, and at time t_i , there are d_i events. Let Y_i be the number of individuals who are at risk at time t_i . The variance of $\hat{S}(t)$, given by the Greenwood formula, is $\hat{\sigma}^2[\hat{S}(t)] = \sigma_S^2(t)\hat{S}^2(t)$, where

$$\sigma_S^2(t) = \sum_{t_i \le t} \frac{d_i}{Y_i(Y_i - d_i)}$$

Let $t_L < t_U$ be the time range for the confidence band so that t_U is less than or equal to the largest event time. For the Hall-Wellner band, t_L can be zero, but for the equal-precision band, t_L is greater

than or equal to the smallest event time. Let

$$a_L = \frac{n\sigma_S^2(t_L)}{1 + n\sigma_S^2(t_L)}$$
 and $a_U = \frac{n\sigma_S^2(t_U)}{1 + n\sigma_S^2(t_U)}$

Let $\{W^0(u), 0 \le u \le 1\}$ be a Brownian bridge.

Hall-Wellner Band

The $100(1-\alpha)\%$ HW band of Hall and Wellner (1980) is

$$\hat{S}(t) - h_{\alpha}(a_L, a_U)n^{-\frac{1}{2}}[1 + n\sigma_S^2(t)]\hat{S}(t) \le S(t) \le \hat{S}(t) + h_{\alpha}(a_L, a_U)n^{-\frac{1}{2}}[1 + n\sigma_S^2(t)]\hat{S}(t)$$

for all $t_L \le t \le t_U$, where $h_{\alpha}(a_L, a_U)$ is given by

$$\alpha = \Pr\{\sup_{a_L \le u \le a_U} |W^0(u)| > h_\alpha(a_L, a_U)\}$$

The critical values are computed from the results in Chung (1986).

Note that the given confidence band has a formula similar to that of the (linear) pointwise confidence interval, where $h_{\alpha}(a_L, a_U)$ and $n^{-\frac{1}{2}}[1+n\sigma_S^2(t)]\hat{S}(t)$ in the former correspond to $z_{\frac{\alpha}{2}}$ and $\hat{\sigma}(\hat{S}(t))$ in the latter, respectively. You can obtain the other transformations (arcsine-square root, log-log, log, and logit) for the confidence bands by replacing $z_{\frac{\alpha}{2}}$ and $\hat{\tau}(t)$ in the corresponding pointwise confidence interval formula by $h_{\alpha}(a_L, a_U)$ and the following $\hat{\tau}(t)$, respectively.

Arcsine-Square Root Transformation

$$\hat{\tau}(t) = \frac{1 + n\sigma_S^2(t)}{2} \sqrt{\frac{S(t)}{n[1 - S(t)]}}$$

Log Transformation

$$\hat{\tau}(t) = \frac{1 + n\sigma_S^2(t)}{\sqrt{n}}$$

Log-Log Transformation

$$\hat{\tau}(t) = \frac{1 + n\sigma_S^2(t)}{\sqrt{n}|\log[\hat{S}(t)]|}$$

Logit Transformation

$$\hat{\tau}(t) = \frac{1 + n\sigma_S^2(t)}{\sqrt{n}[1 - \hat{S}(t)]}$$

Equal-Precision Band

The $100(1-\alpha)\%$ EP band of Nair (1984) is

$$\hat{S}(t) - e_{\alpha}(a_L, a_U)\hat{S}(t)\sigma_S(t) \le S(t) \le \hat{S}(t) + e_{\alpha}(a_L, a_U)\hat{S}(t)\sigma_S(t)$$

for all $t_L \le t \le t_U$, where $e_{\alpha}(a_L, a_U)$ is given by

$$\alpha = \Pr\{\sup_{a_L \le u \le a_U} \frac{|W^0(u)|}{[u(1-u)]^{\frac{1}{2}}} > e_{\alpha}(a_L, a_U)\}$$

PROC LIFETEST uses the approximation of Miller and Siegmund (1982, Equation 8) to approximate the tail probability in which $e_{\alpha}(a_L, a_U)$ is obtained by solving x in

$$\frac{4x\phi(x)}{x} + \phi(x)\left(x - \frac{1}{x}\right)\log\left[\frac{a_U(1 - a_L)}{a_L(1 - a_U)}\right] = \alpha$$

where $\phi(x)$ is the standard normal density function evaluated at x. Note that the confidence bounds given are proportional to the pointwise confidence intervals. As a matter of fact, this confidence band and the (linear) pointwise confidence interval have the same formula except for the critical values $(z_{\frac{\alpha}{2}}$ for the pointwise confidence interval and $e_{\alpha}(a_L, a_U)$ for the band). You can obtain the other transformations (arcsine-square root, log-log, log, and logit) for the confidence bands by replacing $z_{\frac{\alpha}{2}}$ by $e_{\alpha}(a_L, a_U)$ in the formula of the pointwise confidence intervals.

Kernel-Smoothed Hazard Estimate

Kernel-smoothed estimators of the hazard function h(t) are based on the Nelson-Aalen estimator $\tilde{H}(t)$ and its variance $\hat{V}(\tilde{H}(t))$. Consider the jumps of $\tilde{H}(t)$ and $\hat{V}(\tilde{H}(t))$ at the event times $t_1 < t_2 < \ldots < t_D$ as follows:

$$\Delta \tilde{H}(t_i) = \tilde{H}(t_i) - \tilde{H}(t_{i-1})$$

$$\hat{V}(\tilde{H}(t_i)) = \hat{V}(\tilde{H}(t_i)) - \hat{V}(\tilde{H}(t_{i-1}))$$

where $t_0=0$.

The kernel-smoothed estimator of h(t) is a weighted average of $\Delta \tilde{H}(t)$ over event times that are within a bandwidth distance b of t. The weights are controlled by the choice of kernel function, K(), defined on the interval [-1,1]. The choices of K() are as follows:

uniform kernel

$$K_U(x) = \frac{1}{2}, -1 \le x \le 1$$

Epanechnikov kernel

$$K_E(x) = \frac{3}{4}(1 - x^2), -1 \le x \le 1$$

biweight kernel

$$K_{BW}(x) = \frac{15}{16}(1 - x^2)^2, -1 \le x \le 1$$

The kernel-smoothed hazard rate estimator is defined for all time points on $(0, t_D)$. For time points t for which $b \le t \le t_D - b$, the kernel-smoothed estimated of h(t) based on the kernel K() is given by

$$\hat{h}(t) = \frac{1}{b} \sum_{i=1}^{D} K\left(\frac{t - t_i}{b}\right) \Delta \tilde{H}(t_i)$$

The variance of $\hat{h}(t)$ is estimated by

$$\hat{\sigma^2}(\hat{h}(t)) = \frac{1}{b^2} \sum_{i=1}^D K\left(\frac{t-t_i}{b}\right)^2 \Delta \hat{V}(\tilde{H}(t_i))$$

For t < b, the symmetric kernels K() are replaced by the corresponding asymmetric kernels of Gasser and Müller (1979). Let $q = \frac{t}{h}$. The modified kernels are as follows:

uniform kernel

$$K_{U,q}(x) = \frac{4(1+q^3)}{(1+q)^4} + \frac{6(1-q)}{(1+q)^3}x, -1 \le x \le q$$

Epanechnikov kernel

$$K_{E,q}(x) = K_E(x) \frac{64(2 - 4q + 6q^2 - 3q^3) + 240(1 - q)^2 x}{(1 + q)^4 (19 - 18q + 3q^2)}, -1 \le x \le q$$

biweight kernel

$$K_{BW}(x) = K_{BW} \frac{64(8 - 24q + 48q^2 - 45q^3 + 15q^4) + 1120(1 - q)^3 x}{(1 + q)^5 (81 - 168q + 126q^2 - 40q^3 + 5q^4)}, -1 \le x \le q$$

For $t_D - b \le t \le t_D$, let $q = \frac{t_D - t}{b}$. The asymmetric kernels for t < b are used with x replaced by -x.

Using the log transform on the smoothed hazard rate, the $100(1-\alpha)\%$ pointwise confidence interval for the smoothed hazard rate h(t) is given by

$$\hat{h}(t) = \hat{h}(t) \exp\left[\pm \frac{z_{1-\alpha/2}\hat{\sigma}(\hat{h}(t))}{\hat{h}(t)}\right]$$

where $z_{1-\frac{\alpha}{2}}$ is the $100(1-\frac{\alpha}{2})$ th percentile of the standard normal distribution.

Optimal Bandwidth

The following mean integrated squared error (MISE) over the range τ_L and τ_U is used as a measure of the global performance of the kernel function estimator

$$MISE(b) = E \int_{\tau_L}^{\tau_U} (\hat{h}(i) - h(u))^2 du$$

= $E \int_{\tau_L}^{\tau_U} \hat{h}^2(u) du - 2E \int_{\tau_L}^{\tau_U} \hat{h}(u) h(u) du + E \int_{\tau_L}^{\tau_U} h^2(u) du$

The last term is independent of the choice of the kernel and bandwidth and can be ignored when you are looking for the best value of b. The first integral can be approximated by using the trapezoid rule by evaluating $\hat{h}(t)$ at a grid of points $\tau_L = u_1 < ... < u_M = \tau_U$. You can specify τ_L, τ_R , and M by using the options MISEMIN=, MISEMAX=, and MISENUM=, respectively, of the HAZARD plot. The second integral can be estimated by Ramlau-Hansen (1983a, b) cross-validation estimate

$$\frac{1}{b} \sum_{i \neq j} K\left(\frac{t_i - t_j}{b}\right) \Delta \hat{H}(t_i) \Delta \hat{H}(t_j)$$

Therefore, for a fixed kernel, the optimal bandwidth is the quantity b that minimizes

$$g(b) = \sum_{i=1}^{M-1} \left[\frac{u_{i+1} - u_k}{2} \left(\hat{h}^2(u_i) + \hat{h}^2(u_{i+1}) \right) \right] - \frac{2}{b} \sum_{i \neq j} K\left(\frac{t_i - t_j}{b} \right) \Delta \hat{H}(t_i) \Delta \hat{H}(t_j)$$

The minimization is carried out by the golden section search algorithm.

Comparison of Two or More Groups of Survival Data

Let k be the number of groups. Let $S_i(t)$ be the underlying survivor function ith group, i = 1, ..., k. The null and alternative hypotheses to be tested are

$$H_0: S_1(t) = S_2(t) = \ldots = S_k(t)$$
 for all $t \le \tau$

versus

 H_1 : at least one of the $S_i(t)$'s is different for some $t \leq \tau$

respectively, where τ is the largest observed time.

Likelihood Ratio Test

The likelihood ratio test statistic (Lawless 1982) for test H_0 versus H_1 assumes that the data in the various samples are exponentially distributed and tests that the scale parameters are equal. The test statistic is computed as

$$\chi^{2} = 2N \log \left(\frac{T}{N}\right) - 2 \sum_{j=1}^{k} N_{j} \log \left(\frac{T_{j}}{N_{j}}\right)$$

where N_j is the total number of events in the jth stratum, $N = \sum_{j=1}^{k} N_j$, T_j is the total time on test in the jth stratum, and $T = \sum_{j=1}^{k} T_j$. The approximate probability value is computed by treating χ^2 as having a chi-square distribution with k-1 degrees of freedom.

Nonparametric Tests

Let $t_1 < t_2 < \ldots < t_D$ be the distinct event times in the pooled sample. At time t_i , let $W(t_i)$ be a positive weight function, and let n_{ij} and d_{ij} be the size of the risk set and the number of events in the jth sample, respectively. Let $n_i = \sum_{j=1}^k n_{ij}$, $d_i = \sum_{j=1}^k d_{ij}$, and $s_i = n_i - d_i$.

The choices of the weight function $W(t_i)$ are given in Table 49.3.

Table 49.3 Weight Functions for Various Tests

Test	$W(t_i)$
Log-rank	1.0
Wilcoxon	n_i
Tarone-Ware	$\sqrt[\infty]{n_i}$
Peto-Peto	$ ilde{S}(t_i)$
Modified Peto-Peto	$\tilde{S}(t_i) \frac{n_i}{n_i + 1} \\ [\hat{S}(t_i)]^p [1 - \hat{S}(t_i)]^q, p \ge 0, q \ge 0$
Harrington-Fleming (p,q)	$[\hat{S}(t_i)]^p [1 - \hat{S}(t_i)]^q, p \ge 0, q \ge 0$

where $\hat{S}(t)$ is the product-limit estimate at t for the pooled sample, and $\tilde{S}(t)$ is a survivor function estimate close to $\hat{S}(t)$ given by

$$\tilde{S}(t) = \prod_{t_i < t} \left(1 - \frac{d_i}{n_i + 1} \right)$$

Unstratified Tests The rank statistics (Klein and Moeschberger 1997, Section 7.3) for testing H_0 versus H_1 have the form of a k-vector $\mathbf{v} = (v_1, v_2, \dots, v_k)'$ with

$$v_j = \sum_{i=1}^D W(t_i) \left\{ d_{ij} - \frac{n_{ij} d_i}{n_i} \right\}$$

and the estimated covariance matrix, $V = (V_{il})$, is given by

$$V_{jl} = \sum_{i=1}^{D} W^{2}(t_{i}) \left\{ \frac{d_{i} s_{i} (n_{i} n_{il} \delta_{jl} - n_{ij} n_{il})}{n_{i}^{2} (n_{i} - 1)} \right\}$$

where δ_{jl} is 1 if j=l and 0 otherwise. The term v_j can be interpreted as a weighted sum of observed minus expected numbers of failure under the null hypothesis of identical survival curves. The overall test statistic for homogeneity is $\mathbf{v}'\mathbf{V}^-\mathbf{v}$, where \mathbf{V}^- denotes a generalized inverse of \mathbf{V} . This statistic is treated as having a chi-square distribution with degrees of freedom equal to the rank of \mathbf{V} for the purposes of computing an approximate probability level.

Stratified Tests Suppose the test is to be stratified on M levels of a set of STRATA variables. Based only on the data of the sth stratum ($s = 1 \dots M$), let \mathbf{v}_s be the test statistic (Klein and Moeschberger 1997, Section 7.5) for the sth stratum, and let \mathbf{V}_s be its covariance matrix. Let

$$\mathbf{v} = \sum_{s=1}^{M} \mathbf{v}_{s}$$

$$\mathbf{V} = \sum_{s=1}^{M} \mathbf{V}_{s}$$

A global test statistic is constructed as

$$\chi^2 = \mathbf{v}' \mathbf{V} \mathbf{v}$$

Under the null hypothesis, the test statistic has a χ^2 distribution with the same degrees of freedom as the individual test for each stratum.

Multiple-Comparison Adjustments Let χ_r^2 denote a chi-squared random variable with r degrees of freedom. Denote ϕ and Φ as the density function and the cumulative distribution function of a standard normal distribution, respectively. Let m be the number of comparisons; that is,

$$m = \begin{cases} \frac{k(k-1)}{2} & \text{DIFF} = \text{ALL} \\ k-1 & \text{DIFF} = \text{CONTROL} \end{cases}$$

For a two-sided test comparing the survival of the j th group with that of lth group, $1 \le j \ne l \le r$, the test statistic is

$$z_{jl}^2 = \frac{(v_j - v_l)^2}{V_{ij} + V_{II} - 2V_{iI}}$$

and the raw p-value is

$$p = \Pr(\chi_1^2 > z_{il}^2)$$

Adjusted *p*-values for various multiple-comparison adjustments are computed as follows:

Bonferroni Adjustment

$$p = \min\{1, m\Pr(\chi_1^2 > z_{il}^2)\}$$

Dunnett-Hsu Adjustment

With the first group being the control, let $C = (c_{ij})$ be the $(r-1) \times r$ matrix of contrasts; that is,

$$c_{ij} = \begin{cases} 1 & i = 1, \dots, r - 1, j = 2, \dots, r \\ -1 & j = i + 1, i = 2, \dots, r \\ 0 & \text{otherwise} \end{cases}$$

Let $\Sigma \equiv (\sigma_{ij})$ and $\mathbf{R} \equiv (r_{ij})$ be covariance and correlation matrices of $\mathbf{C}\mathbf{v}$, respectively; that is,

$$\Sigma = CVC'$$

and

$$r_{ij} = \frac{\sigma_{ij}}{\sqrt{\sigma_{ii}\sigma_{jj}}}$$

The factor-analytic covariance approximation of Hsu (1992) is to find $\lambda_1, \ldots, \lambda_{r-1}$ such that

$$\mathbf{R} = \mathbf{D} + \lambda \lambda'$$

where **D** is a diagonal matrix with the *j*th diagonal element being $1 - \lambda_j$ and $\lambda = (\lambda_1, \dots, \lambda_{r-1})'$. The adjusted *p*-value is

$$p = 1 - \int_{-\infty}^{\infty} \phi(y) \prod_{i=1}^{r-1} \left[\Phi\left(\frac{\lambda_i y + z_{jl}}{\sqrt{1 - \lambda_i^2}}\right) - \Phi\left(\frac{\lambda_i y - z_{jl}}{\sqrt{1 - \lambda_i^2}}\right) \right] dy$$

which can be obtained in a DATA step as

$$p = \text{PROBMC}(\text{"DUNNETT2"}, z_{ii}, ..., r-1, \lambda_1, ..., \lambda_{r-1}).$$

Scheffé Adjustment

$$p = \Pr(\chi_{r-1}^2 > z_{jl}^2)$$

Šidák Adjustment

$$p = 1 - \{1 - \Pr(\chi_1^2 > z_{jl}^2)\}^m$$

SMM Adjustment

$$p = 1 - [2\Phi(z_{il}) - 1]^m$$

which can also be evaluated in a DATA step as

$$p = 1 - \text{PROBMC}(\text{"MAXMOD"}, z_{il}, ..., m).$$

Tukey Adjustment

$$p = 1 - \int_{-\infty}^{\infty} r\phi(y) [\Phi(y) - \Phi(y - \sqrt{2}z_{jl})]^{r-1} dy$$

which can also be evaluated in a DATA step as

$$p = 1 - \text{PROBMC}(\text{"RANGE"}, \sqrt{2}z_{il}, ., ., r).$$

Trend Tests Trend tests (Klein and Moeschberger 1997, Section 7.4) have more power to detect ordered alternatives as

$$H_2: S_1(t) \geq S_2(t) \geq \ldots \geq S_k(t), t \leq \tau$$
, with at least one inequality

or

$$H_2: S_1(t) \leq S_2(t) \leq \ldots \leq S_k(t), t \leq \tau$$
, with at least one inequality

Let $a_1 < a_2 < \ldots < a_k$ be a sequence of scores associated with the k samples. The test statistic and its standard error are given by $\sum_{j=1}^k a_j v_j$ and $\sum_{j=1}^k \sum_{l=1}^k a_j a_l V_{jl}$, respectively. Under H_0 , the z-score

$$Z = \frac{\sum_{j=1}^{k} a_j v_j}{\sqrt{\{\sum_{i=1}^{k} \sum_{l=1}^{k} a_j a_l V_{jl}\}}}$$

has, asymptotically, a standard normal distribution. PROC LIFETEST provides both one-tail and two-tail *p*-values for the test.

Rank Tests for the Association of Survival Time with Covariates

The rank tests for the association of covariates (Kalbfleisch and Prentice 1980, Chapter 6) are more general cases of the rank tests for homogeneity. In this section, the index α is used to label all observations, $\alpha = 1, 2, ..., n$, and the indices i, j range only over the observations that correspond to events, i, j = 1, 2, ..., k. The ordered event times are denoted as $t_{(i)}$, the corresponding vectors of covariates are denoted as $\mathbf{z}_{(i)}$, and the ordered times, both censored and event times, are denoted as t_{α} .

The rank test statistics have the form

$$\mathbf{v} = \sum_{\alpha=1}^{n} c_{\alpha,\delta_{\alpha}} \mathbf{z}_{\alpha}$$

where n is the total number of observations, $c_{\alpha,\delta_{\alpha}}$ are rank scores, which can be either log-rank or Wilcoxon rank scores, δ_{α} is 1 if the observation is an event and 0 if the observation is censored, and \mathbf{z}_{α} is the vector of covariates in the TEST statement for the α th observation. Notice that the scores, $c_{\alpha,\delta_{\alpha}}$, depend on the censoring pattern and that the terms are summed up over all observations.

The log-rank scores are

$$c_{\alpha,\delta_{\alpha}} = \sum_{(j:t_{(j)} \le t_{\alpha})} \left(\frac{1}{n_{j}} - \delta_{\alpha} \right)$$

and the Wilcoxon scores are

$$c_{\alpha,\delta_{\alpha}} = 1 - (1 + \delta_{\alpha}) \prod_{(j:t_{(j)} \le t_{\alpha})} \frac{n_j}{n_j + 1}$$

where n_j is the number at risk just prior to $t_{(j)}$.

The estimates used for the covariance matrix of the log-rank statistics are

$$\mathbf{V} = \sum_{i=1}^{k} \frac{\mathbf{V}_i}{n_i}$$

where V_i is the corrected sum of squares and crossproducts matrix for the risk set at time $t_{(i)}$; that is,

$$\mathbf{V}_i = \sum_{(\alpha:t_{\alpha} \geq t_{(i)})} (\mathbf{z}_{\alpha} - \bar{\mathbf{z}}_i)'(\mathbf{z}_{\alpha} - \bar{\mathbf{z}}_i)$$

where

$$\bar{\mathbf{z}}_i = \sum_{(\alpha: t_{\alpha} \ge t_{(i)})} \frac{\mathbf{z}_{\alpha}}{n_i}$$

The estimate used for the covariance matrix of the Wilcoxon statistics is

$$\mathbf{V} = \sum_{i=1}^{k} \left[a_i (1 - a_i^*) (2\mathbf{z}_{(i)}\mathbf{z}'_{(i)} + \mathbf{S}_i) - (a_i^* - a_i) \left(a_i \mathbf{x}_i \mathbf{x}'_i + \sum_{j=i+1}^{k} a_j (\mathbf{x}_i \mathbf{x}'_j + \mathbf{x}_j \mathbf{x}'_i) \right) \right]$$

where

$$a_{i} = \prod_{j=1}^{i} \frac{n_{j}}{n_{j}+1}$$

$$a_{i}^{*} = \prod_{j=1}^{i} \frac{n_{j}+1}{n_{j}+2}$$

$$\mathbf{S}_{i} = \sum_{(\alpha:t_{(i+1)}>t_{\alpha}>t_{(i)})} \mathbf{z}_{\alpha}\mathbf{z}_{\alpha}'$$

$$\mathbf{x}_{i} = 2\mathbf{z}_{(i)} + \sum_{(\alpha:t_{(i+1)}>t_{\alpha}>t_{(i)})} \mathbf{z}_{\alpha}$$

In the case of tied failure times, the statistics \mathbf{v} are averaged over the possible orderings of the tied failure times. The covariance matrices are also averaged over the tied failure times. Averaging the covariance matrices over the tied orderings produces functions with appropriate symmetries for the tied observations; however, the actual variances of the \mathbf{v} statistics would be smaller than the preceding estimates. Unless the proportion of ties is large, it is unlikely that this will be a problem.

The univariate tests for each covariate are formed from each component of \mathbf{v} and the corresponding diagonal element of \mathbf{V} as v_i^2/V_{ii} . These statistics are treated as coming from a chi-square distribution for calculation of probability values.

The statistic $\mathbf{v}'\mathbf{V}^-\mathbf{v}$ is computed by sweeping each pivot of the V matrix in the order of greatest increase to the statistic. The corresponding sequence of partial statistics is tabulated. Sequential

increments for including a given covariate and the corresponding probabilities are also included in the same table. These probabilities are calculated as the tail probabilities of a chi-square distribution with one degree of freedom. Because of the selection process, these probabilities should not be interpreted as *p*-values.

If desired for data screening purposes, the output data set requested by the OUTTEST= option can be treated as a sum of squares and crossproducts matrix and processed by the REG procedure by using the option METHOD=RSQUARE. Then the sets of variables of a given size can be found that give the largest test statistics. Output 49.1 illustrates this process.

Computer Resources

The data are first read and sorted into strata. If the data are originally sorted by failure time and censoring state, with smaller failure times coming first and event values preceding censored values in cases of ties, the data can be processed by strata without additional sorting. Otherwise, the data are read into memory by strata and sorted.

Memory Requirements

For a given BY group, define the following:

- N the total number of observations
- V the number of STRATA variables
- C the number of covariates listed in the TEST statement
- L total length of the ID variables in bytes
- S number of strata
- *n* maximum number of observations within strata

$$b 12 + 8C + L$$

$$m1 (112 + 16V) \times S$$

$$m2 50 \times b \times S$$

$$m3 (50+n) \times (b+4)$$

$$m4 8(C+4)^2$$

$$m5 20N + 8S \times (S+4)$$

The memory, in bytes, required to process the BY group is at least

$$m1 + \max(m2, m3) + m4$$

The test of equality of survival functions across strata requires additional memory (m5 bytes). However, if this additional memory is not available, PROC LIFETEST skips the test for equality of survival functions and finishes the other computations. Additional memory is required for the PLOTS= option. Temporary storage of 16n bytes is required to store the product-limit estimates for plotting.

Output Data Sets

OUTSURV= Data Set

You can specify the OUTSURV= option in the PROC LIFETEST statement to create an output data set containing the following columns:

- any specified BY variables
- any specified STRATA variables, their values coming from either their original values or the midpoints of the stratum intervals if endpoints are used to define strata (semi-infinite intervals are labeled by their finite endpoint)
- STRATUM, a numeric variable that numbers the strata
- the time variable as given in the TIME statement. For METHOD=KM, METHOD=BRESLOW, or METHOD=FH, it contains the observed failure or censored times. For the life-table estimates, it contains the lower endpoints of the time intervals.
- SURVIVAL, a variable containing the survivor function estimates
- CONFTYPE, a variable containing the name of the transformation applied to the survival time
 in the computation of confidence intervals (if the OUT= option is specified in the SURVIVAL
 statement)
- SDF_LCL, a variable containing the lower limits of the pointwise confidence intervals for the survivor function
- SDF_UCL, a variable containing the upper limits of the pointwise confidence intervals for the survivor function

If the estimation uses the product-limit, Breslow, or Fleming-Harrington method, then the data set also contains the following:

• _CENSOR_, an indicator variable that has a value 1 for a censored observation and a value 0 for an event observation

- SDF_STDERR, a variable containing the standard error of the survivor function estimator (if the STDERR option is specified in the PROC LIFETEST statement)
- HW_LCL, a variable containing the lower limits of the Hall-Wellner confidence bands (if the CONFBAND=HW option or the CONFBAND=ALL option is specified in the PROC LIFETEST statement)
- HW_UCL, a variable containing the upper limits of the Hall-Wellner confidence bands (if the CONFBAND=HW option or the CONFBAND=ALL option is specified in the PROC LIFETEST statement)
- EP_LCL, a variable containing the lower limits of the equal-precision confidence bands (if the CONFBAND=EP option or the CONFBAND=ALL option is specified in the PROC LIFETEST statement)
- EP_UCL, a variable containing the upper limits of the equal-precision confidence bands (if the CONFBAND=EP option or the CONFBAND=ALL option is specified in the PROC LIFETEST statement)

If the estimation uses the life-table method, then the data set also contains the following:

- MIDPOINT, a variable containing the value of the midpoint of the time interval
- PDF, a variable containing the density function estimates
- PDF_LCL, a variable containing the lower endpoints of the PDF confidence intervals
- PDF_UCL, a variable containing the upper endpoints of the PDF confidence intervals
- HAZARD, a variable containing the hazard estimates
- HAZ_LCL, a variable containing the lower endpoints of the hazard confidence intervals
- HAZ UCL, a variable containing the upper endpoints of the hazard confidence intervals

Each survival function contains an initial observation with the value 1 for the SDF and the value 0 for the time. The output data set contains an observation for each distinct failure time if the product-limit, Breslow, or Fleming-Harrington method is used, or it contains an observation for each time interval if the life-table method is used. The product-limit, Breslow, or Fleming-Harrington survival estimates are defined to be right continuous; that is, the estimates at a given time include the factor for the failure events that occur at that time.

Labels are assigned to all the variables in the output data set except the BY variable and the STRATA variable.

OUTTEST= Data Set

The OUTTEST= option in the LIFETEST statement creates an output data set containing the rank statistics for testing the association of failure time with covariates. It contains the following:

- any specified BY variables
- _TYPE_, a character variable of length 8 that labels the type of rank test, either "LOG-RANK" or "WILCOXON"
- _NAME_, a character variable of length 8 that labels the rows of the covariance matrix and the test statistics
- the TIME variable, containing the overall test statistic in the observation that has _NAME_ equal to the name of the time variable and the univariate test statistics under their respective covariates.
- all variables listed in the TEST statement

The output is in the form of a symmetric matrix formed by the covariance matrix of the rank statistics bordered by the rank statistics and the overall chi-square statistic. If the value of <code>NAME_</code> is the name of a variable in the TEST statement, the observation contains a row of the covariance matrix and the value of the rank statistic in the time variable. If the value of <code>NAME_</code> is the name of the TIME variable, the observation contains the values of the rank statistics in the variables from the TEST list and the value of the overall chi-square test statistic in the TIME variable.

Two complete sets of statistics labeled by the _TYPE_ variable are produced, one for the log-rank test and one for the Wilcoxon test.

Displayed Output

If you use the NOPRINT option in the PROC LIFETEST statement, the procedure does not display any output.

Product-Limit Survival Estimates

The "Product-Limit Survival Estimates" table is displayed if you request the product-limit method of estimation. The table displays the following:

- the observed (event or censored) time
- the number of units at risk (if you specify the ATRISK option in the PROC LIFETEST statement)
- the number of events (if you specify the ATRISK option in the PROC LIFETEST statement)
- the product-limit estimate of the survivor function
- the corresponding estimate of the cumulative distribution function of the failure time
- the standard error estimate of the survivor function estimator

- the Nelson-Aalen cumulative hazard function estimate (if the NELSON option is specified in the PROC LIFETEST statement)
- the standard error of the Nelson-Aalen estimator (if the NELSON option is specified in the PROC LIFETEST statement)
- the number of event times that have been observed
- the number of event or censored times that remain to be observed
- the frequency of the observed times (if you specify the FREQ statement)
- values of the ID variables (if you specify the ID statement)

For ODS purposes, the name of this table is "ProductLimitEstimates."

Breslow Survival Estimates

The "Breslow Survival Estimates" table is displayed if you request the Breslow method of estimation. The table displays the following:

- the observed (event or censored) time
- the number of units at risk (if you specify the ATRISK option in the PROC LIFETEST statement)
- the number of events (if you specify the ATRISK option in the PROC LIFETEST statement)
- the Breslow estimate of the survivor function
- the corresponding estimate of the cumulative distribution function of the failure time
- the standard error estimate of the survivor function estimator
- the Nelson-Aalen cumulative hazard function estimate (if the NELSON option is specified in the PROC LIFETEST statement)
- the standard error of the Nelson-Aalen estimator (if the NELSON option is specified in the PROC LIFETEST statement)
- the number of event times that have been observed
- the number of event or censored times that remain to be observed
- the frequency of the observed times (if you specify the FREQ statement)
- values of the ID variables (if you specify the ID statement)

For ODS purposes, the name of this table is "BreslowEstimates."

Fleming-Harrington Survival Estimates

The "Fleming-Harrinton Survival Estimates" table is displayed if you request the Fleming-Harrington method of estimation. The table displays the following:

- the observed (event or censored) time
- the number of units at risk (if you specify the ATRISK option in the PROC LIFETEST statement)
- the number of events (if you specify the ATRISK option in the PROC LIFETEST statement)
- the Fleming-Harrington estimate of the survivor function
- the corresponding estimate of the cumulative distribution function of the failure time
- the standard error estimate of the survivor function estimator
- the Nelson-Aalen cumulative hazard function estimate (if the NELSON option is specified in the PROC LIFETEST statement)
- the standard error of the Nelson-Aalen estimator (if the NELSON option is specified in the PROC LIFETEST statement)
- the number of event times that have been observed
- the number of event or censored times that remain to be observed
- the frequency of the observed times (if you specify the FREQ statement)
- values of the ID variables (if you specify the ID statement)

For ODS purposes, the name of this table is "FlemingEstimates."

Quartile Estimates

The "Quartiles Estimates" table is displayed if you request the product-limit, Breslow, or Fleming-Harrington method of estimation. The table displays the following:

- point estimates of the quartiles of the survival times
- the lower and upper confidence limits for the quartiles

For ODS purposes, the name of this table is "Quartiles."

Mean Estimate

The "Mean Estimate" table is displayed if you request the product-limit, Breslow, or Fleming-Harrington method of estimation. The table displays the following:

- the estimated mean survival time
- the estimated standard error of the mean estimator

For ODS purposes, the name of this table is "Means."

Life-Table Survival Estimates

The "Life-Table Survival Estimates" table is displayed if you request the life-table method of estimation. The table displays the following:

- the time intervals into which the failure and censored times are distributed. Each interval is from the lower limit, up to but not including the upper limit; if the upper limit is infinity, the missing value is printed.
- the number of events that occur in the interval
- the number of censored observations that fall into the interval
- the effective sample size for the interval
- the estimate of conditional probability of events (failures) in the interval
- the standard error of the conditional probability estimator
- the estimate of the survival function at the beginning of the interval
- the estimate of the cumulative distribution function of the failure time at the beginning of the interval
- the standard error estimate of the survivor function estimator
- the estimate of the median residual lifetime, which is the amount of time elapsed before reducing the number of at-risk units to one-half. This is also known as the *median future lifetime* in Elandt-Johnson and Johnson (1980)).
- the estimated standard error of the median residual lifetime estimator
- the density function estimated at the midpoint of the interval
- the standard error estimate of the density estimator
- the hazard rate estimated at the midpoint of the interval
- the standard error estimate of the hazard estimator

For ODS purposes, the name of this table is "LifetableEstimates."

Summary of the Number of Censored and Uncensored Values

The "Summary of the Number of Censored and Uncensored Values" table displays following:

- the stratum identification (if the STRATA statement is specified)
- the total number of observations.
- the number of event observations,
- the number of censored observations, and
- the percentage of censored observations.

For ODS purposes, the name of this table is "CensoredSummary."

Rank Statistics

The "Rank Statistics" table contains the test statistics of the nonparametric *k*-sample tests. For ODS purposes, the name of this table is "HomStats."

Covariance Matrix for the Log-Rank Statistics

The "Covariance Matrix for the Log-Rank Statistics" table is displayed if the log-rank *k*-sample test is requested. For ODS purposes, the name of this table is "LogrankHomCov."

Covariance Matrix for the Wilcoxon Statistics

The "Covariance Matrix for the Wilcoxon Statistics" table is displayed if the Wilcoxon *k*-sample test is requested. For ODS purposes, the name of this table is "WilHomCov."

Covariance Matrix for the Tarone Statistics

The "Covariance Matrix for the Tarone Statistics" table is displayed if the Tarone-Ware *k*-sample test is requested. For ODS purposes, the name of this table is "TaroneHomCov."

Covariance Matrix for the Peto Statistics

The "Covariance Matrix for the Peto Statistics" table is displayed if the Peto-Peto *k*-sample test is requested. For ODS purposes, the name of this table is "PetoHomCov."

Covariance Matrix for the ModPeto Statistics

The "Covariance Matrix for the ModPeto Statistics" table is displayed if the modified Peto-Peto *k*-sample test is requested. For ODS purposes, the name of this table is "ModPetoHomCov."

Covariance Matrix for the Fleming Statistics

The "Covariance Matrix for the Fleming Statistics" table is displayed if the Fleming-Harrington *k*-sample test is requested. For ODS purposes, the name of this table is "FlemingHomCov."

Test of Equality over Strata

The "Test of Equality over Strata" table is displayed if an unstratified *k*-sample test is carried out. The table contains the chi-square statistics, degrees of freedom, and *p*-values of the nonparametric tests and the likelihood ratio test (which is based on the exponential distribution). For ODS purposes, the name of this table is "HomTests."

Stratified Test of Equality over Group

The "Stratified Test of Equality over Group" table is displayed if a stratified test is carried out. The tables contains the chi-square statistics, degrees of freedom, and *p*-values of the stratified tests. For ODS purposes, the name of this table is "HomTests."

Scores for Trend Test

The "Scores for Trend Test" table is displayed if the TREND option is specified in the STRATA statement. The table contains the set of scores used to construct the trend tests. For ODS purposes, the name of this table is "TrendScores."

Trend Tests

The "Trend Tests" table is displayed if the TREND option is specified in the STRATA statement. The table contains the results of the trend tests. For ODS purposes, the name of this table is "TrendTests."

Adjustment for Multiple Comparisons for the Log-Rank Test

The "Adjustment for Multiple Comparisons for the Log-Rank Test" table is displayed if the log-rank test and a multiple-comparison adjustment method are specified. The table contains the chi-square statistics and the raw and adjusted *p*-values of the paired comparisons. For ODS purposes, the name of this table is "SurvDiff."

Adjustment for Multiple Comparisons for the Wilcoxon Test

The "Adjustment for Multiple Comparisons for the Wilcoxon Test" table is displayed if the Wilcoxon test and a multiple-comparison method are specified. The table contains the chi-square statistics and the raw and adjusted *p*-values of the paired comparisons. For ODS purposes, the name of this table is "SurvDiff."

Adjustment for Multiple Comparisons for the Tarone Test

The "Adjustment for Multiple Comparisons for the Tarone Test" table is displayed if the Tarone-Ware test and a multiple-comparison method are specified. The table contains the chi-square statistics and the raw and adjusted *p*-values of the paired comparisons. For ODS purposes, the name of this table is "SurvDiff."

Adjustment for Multiple Comparisons for the Peto Test

The "Adjustment for Multiple Comparisons for the Peto Test" table is displayed if the Peto-Peto test and a multiple-comparison method are specified. The table contains the chi-square statistics and the raw and adjusted *p*-values of the paired comparisons. For ODS purposes, the name of this table is "SurvDiff."

Adjustment for Multiple Comparisons for the ModPeto Test

The "Adjustment for Multiple Comparisons for the ModPeto Test" table is displayed if the modified Peto-Peto test and a multiple-comparison method are specified. The table contains the chi-square statistics and the raw and adjusted *p*-values of the paired comparisons. For ODS purposes, the name of this table is "SurvDiff."

Adjustment for Multiple Comparisons for the Fleming Test

The "Adjustment for Multiple Comparisons for the Fleming Test" table is displayed if the Fleming-Harrington test and a multiple-comparison method are specified. The table contains the chi-square statistics and the raw and adjusted *p*-values of the paired comparisons. For ODS purposes, the name of this table is "SurvDiff."

Univariate Chi-Squares for the Log-Rank Test

The "Univariate Chi-Squares for the Log-Rank Test" table is displayed if the TEST statement is specified. The table displays the log-rank test results for individual variables in the TEST statement. For ODS purposes, the name of this table is "LogUniChiSq."

Covariance Matrix of the Log-Rank Statistics

The "Covariance Matrix of the Log-Rank Statistics" table is displayed if the TEST statement is specified. The table displays the estimated covariance matrix of the log-rank statistics for association. For ODS purposes, the name of this table is "LogTestCov."

Forward Stepwise Sequence of Chi-Squares for the Log-Rank Test

The "Forward Stepwise Sequence of Chi-Squares for the Log-Rank Test" table is displayed if the TEST statement is specified. The table contains the sequence of partial chi-square statistics for the log-rank test in the order of the greatest increase to the overall test statistic, the degrees of freedom of the partial chi-square statistics, the approximate probability values of the partial chi-square statistics, the chi-square increments for including the given variables, and the probability values of the chi-square increments. For ODS purposes, the name of this table is "LogForStepSeq."

Univariate Chi-Squares for the Wilcoxon Test

The "Univariate Chi-Squares for the Wilcoxon Test" table displays the Wilcoxon test results for individual variables in the TEST statement. For ODS purposes, the name of this table is "WilUniChiSq."

Covariance Matrix of the Wilcoxon Statistics

The "Covariance Matrix of the Wilcoxon Statistics" table is displayed if the TEST statement is specified. The table displays the estimated covariance matrix of the Wilcoxon statistics for association. For ODS purposes, the name of this table is "WilTestCov."

Forward Stepwise Sequence of Chi-Squares for the Wilcoxon Test

The "Forward Stepwise Sequence of Chi-Squares for the Wilcoxon Test" table is displayed if the TEST statement is specified. The table contains the sequence of partial chi-square statistics for the Wilcoxon test in the order of the greatest increase to the overall test statistic, the degrees of freedom of the partial chi-square statistics, the approximate probability values of the partial chi-square statistics, the chi-square increments for including the given variables, and the probability values of the chi-square increments. For ODS purposes, the name of this table is "WilForStepSeq."

ODS Table Names

PROC LIFETEST assigns a name to each table it creates. You can use these names to reference the table when using the Output Delivery System (ODS) to select tables and create output data sets. These names are listed in Table 49.4. For more information about ODS, see Chapter 20, "Using the Output Delivery System."

Table 49.4 ODS Tables Produced by PROC LIFETEST

ODS Table Name	Description	Statement / Option
BreslowEstimates	Breslow estimates	PROC LIFETEST METHOD=B
CensoredSummary	Number of event and censored ob-	PROC LIFETEST
	servations	METHOD=PL Ã FH
FlemingEstimates	Fleming-Harrington estimates	PROC LIFETEST
		METHOD=FH
FlemingHomCov	Covariance matrix for <i>k</i> -sample FLEMING statistics	STRATA / TEST=FLEMING
HomStats	Test statistics for <i>k</i> -sample tests	STRATA / TEST=
HomTests	Results of <i>k</i> -sample tests	STRATA / TEST=
LifetableEstimates	Life-table survival estimates	PROC LIFETEST
		METHOD=LT
LogForStepSeq	Forward stepwise sequence for	TEST /
	the log-rank statistics for associa-	
	tion	
LogHomCov	Covariance matrix for <i>k</i> -sample	STRATA / TEST=LOGRANK
	LOGRANK statistics	
LogTestCov	Covariance matrix for log-rank	TEST /
	statistics for association	
LogUniChisq	Univariate chi-squares for log-	TEST /
	rank statistics for association	
Means	Mean and standard error of sur-	PROC LIFETEST
	vival times	METHOD=PL
ModPetoHomCov	Covariance matrix for <i>k</i> -sample	STRATA / TEST=MODPETO
	MODPETO statistics	
PetoHomCov	Covariance matrix for <i>k</i> -sample	STRATA / TEST=PETO
	PETO statistics	
ProductLimitEstimates	Product-limit survival estimates	PROC LIFETEST
		METHOD=PL
Quartiles	Quartiles of the survival times	PROC LIFETEST
		METHOD=PL B FH
SurvDiff	Adjustments for multiple comparisons	STRATA / ADJUST= & DIFF=
TaroneHomCov	Covariance matrix for <i>k</i> -sample TARONE statistics	STRATA / TEST=TARONE
TrendScores	Scores used to construct trend	STRATA / TREND
	tests	
TrendTests	Results of trend tests	STRATA / TREND
WilForStepSeq	Forward stepwise sequence for	TEST /
1 1	the log-rank statistics for association	
WilHomCov	Covariance matrix for <i>k</i> -sample	STRATA / TEST=WILCOXON
··· mionicov	WILCOXON statistics	STRUIT, ILST-WILCONON
WilTestCov	Covariance matrix for log-rank	TEST /
	statistics for association	

Table 49.4 continued

ODS Table Name	Description	Statement / Option
WilUniChiSq	Univariate chi-squares for Wilcoxon statistics for association	

ODS Graphics

This section describes the use of ODS for creating statistical graphs with the LIFETEST procedure. To request these graphs you must specify the ODS GRAPHICS ON statement. See Chapter 21, "Statistical Graphics Using ODS," for more information. The survival plot is produced by default; other graphs are produced by using the PLOTS= option in the PROC LIFETEST statement. You can reference every graph produced through ODS Graphics with a name. The names of the graphs that PROC LIFETEST generates are listed in Table 49.5, along with the required keywords for the PLOTS= option.

 Table 49.5
 ODS Graphics Produced by PROC LIFETEST

ODS Graph Name	Plot Description	PLOTS=Option
DensityPlot	Estimated density for life-table method	PDF
FailurePlot	Estimated failure function	SURVIVAL(FAILURE)
HazardPlot	Estimated hazard function for life-table method or smoothed hazard for product-	HAZARD
	limit, Breslow, or Fleming-Harrington method	
LogNegLogSurvivalPlot	Log of negative log of the estimated survivor function	LOGLOGS
NegLogSurvivalPlot	Negative log of the estimated survivor function	LOGSURV
SurvivalPlot	Estimated survivor function	SURVIVAL
SurvivalPlot	Estimated survivor function with number of subjects at risk	SURVIVAL(ATRISK=)
SurvivalPlot	Estimated survivor function with pointwise confidence limits	SURVIVAL(CL)
SurvivalPlot	Estimated survivor function with equal- precision band	SURVIVAL(CB=EP)
SurvivalPlot	Estimated survivor function with Hall-Wellner band	SURVIVAL(CB=HW)
SurvivalPlot	Estimated survivor function with homogeneity test <i>p</i> -value	SURVIVAL(TEST)

Additional Dynamic Variables for Survival Plots Using ODS Graphics

PROC LIFETEST passes a number of summary statistics as dynamic variables to the ODS Graphics for survival plots. Table 49.6 and Table 49.7 list these additional dynamic variables for the Kaplan-Meier curves and the life-table curves, respectively. These dynamic variables are not declared in the templates for the survival curves, but you can declare them and use them to enhance the default plots. The names of the dynamic variables depend on the STRATA= suboption of the PLOTS=SURVIVAL option: STRATA=INDIVIDUAL produces a separate plot for each stratum, and STRATA=OVERALL produces one plot with overlaid curves.

Table 49.6 Additional Dynamic Variables for Stat. Graphics. ProductLimitSurvival

STRATA=	Dynamic	Description
OVERLAY	StrVal j	Label for the <i>j</i> th stratum
	NObs j	Number of observations in the j th stratum
	NEvent j	Number of events in the j th stratum
	Median j	Median survival time of the j th stratum
	LowerMedian j	Lower median survival time of the j th stratum
	UpperMedian j	Upper median survival time of the j th stratum
	pctMedianConfid	Percent confidence of the median intervals
INDIVIDUAL	NObs	Number of observations
	NEvent	Number of events
	Median	Median survival time
	LowerMedian	Lower median survival time
	UpperMedian	Upper median survival time
	pctMedianConfid	Percent confidence of the median interval

Table 49.7 Additional Dynamic Variables for Stat.Graphics.LifetableSurvival

STRATA=	Dynamic	Description
OVERLAY	StrVal j	Label for the <i>j</i> th stratum
	NObs <i>j</i>	Number of observations in the j th stratum
	NEvent j	Number of events in the j th stratum
INDIVIDUAL	NObs	Number of observations
	NEvent	Number of events

See the section "The Graph Template Language" on page 687 and Example 21.5 in Chapter 21, "Statistical Graphics Using ODS," for more information about dynamic variables and ODS Graphics.

Examples: LIFETEST Procedure

Example 49.1: Product-Limit Estimates and Tests of Association

The data presented in Appendix I of Kalbfleisch and Prentice (1980) are coded in the following DATA step. The response variable, SurvTime, is the survival time in days of a lung cancer patient. Negative values of SurvTime are censored values. The covariates are Cell (type of cancer cell), Therapy (type of therapy: standard or test), Prior (prior therapy: 0=no, 10=yes), Age (age in years), DiagTime (time in months from diagnosis to entry into the trial), and Kps (performance status). A censoring indicator variable Censor is created from the data, with the value 1 indicating a censored time and the value 0 indicating an event time. Since there are only two types of therapy, an indicator variable, Treatment, is constructed for therapy type, with value 0 for standard therapy and value 1 for test therapy.

```
data VALung;
  drop check m;
  retain Therapy Cell;
  infile cards column=column;
  length Check $ 1;
  label SurvTime='failure or censoring time'
     Kps='karnofsky index'
     DiagTime='months till randomization'
     Age='age in years'
     Prior='prior treatment?'
     Cell='cell type'
     Therapy='type of treatment'
     Treatment='treatment indicator';
  M=Column;
  input Check $ @@;
  if M>Column then M=1;
  if Check='s'|Check='t' then input @M Therapy $ Cell $ ;
  else input @M SurvTime Kps DiagTime Age Prior @@;
  if SurvTime > .;
  censor=(SurvTime<0);</pre>
  SurvTime=abs(SurvTime);
  Treatment=(Therapy='test');
  datalines;
standard squamous
72 60 7 69 0 411 70 5 64 10 228 60 3 38 0 126 60 9 63 10
314 50 18 43 0 -100 70 6 70 0 42 60 4 81 0 8 40 58 63 10
144 30 4 63 0 -25 80 9 52 10 11 70 11 48 10
standard small
30 60 3 61 0 384 60 9 42 0 4 40 2 35 0 54 80 4 63 10
```

13	60	4	56	0	-123	40	3	55	0	-97	60	5	67	0	153	60	14	63	10
59	30	2	65	0	117	80	3	46	0	16	30	4	53	10	151	50	12	69	0
22	60	4	68	0	56	80	12	43	10	21	40	2	55	10	18	20	15	42	0
139	80	2	64	0	20	30	5	65	0	31	75	3	65	0	52	70	2	55	0
287	60	25	66	10	18	30	4	60	0	51	60	1	67	0	122	80	28	53	0
27	60	8	62	0	54	70	1	67	0	7	50	7	72	0	63	50	11	48	0
392	40	4	68	0	10	40	23	67	10										
star	nda	rd a	ade	no															
8	20	19	61	10	92	70	10	60	0	35	40	6	62	0	117	80	2	38	0
132	80	5	50	0	12	50	4	63	10	162	80	5	64	0	3	30	3	43	0
95	80	4	34	0															
star	nda	rd I	Lar	ge															
177	50	16	66	10	162	80	5	62	0	216	50	15	52	0	553	70	2	47	0
278	60	12	63	0	12	40	12	68	10	260	80	5	45	0	200	80	12	41	10
156	70	_	66	0	-182		_	62	0	143		8	60	0	105	80	11	66	0
103	80	5	38	0	250	70	8	53	10	100	60	13	37	10					
test		_																	
999			_		112			60	0	-87			48	0	-231		_	52	
242			70	0	991			50		111			62	0			21		10
587			58	0	389			62	0		30		64	0	_		36		0
357				0	467		_	64	0	201						50	7	35	0
30	70	11	63	0	44	60	13	70	10	283	90	2	51	0	15	50	13	40	10
test																			
_	30		69	0	-103						20		71	0	_	30		62	0
_	60		60	0			36				30		54				11		0
	60	-	49	0		70	3	72	0	_	80	_	68	0		85	4	62	0
	70	_	71	0	25	70	2	70	0	95	70	1	61	0	80	50	17	71	0
		87		10	29	40	8	67	0										
test				_			_					_		_			_		_
	40		60	0		40	_	69		-83			57	0	_	80		39	0
_	60	_	62	0			22			_	60		43	0	_	60		70	0
_	50	5		0	36	70	8		0		10	4	-	0	7		4	58	0
140			63	0	186		3		0	84	80	4	62	10	19	50	10	42	0
_	40	_	69	0	80	40	4	63	0										
test		_																	
_	60		45	0	164				10		30		39			60		66	0
_	30		63	0			11			340				10	133		1	65	0
111	60	5	64	0	231	70	18	67	10	378	80	4	65	0	49	30	3	37	0
;																			

In the following statements, PROC LIFETEST is invoked to compute the product-limit estimate of the survivor function for each type of cancer cell and to analyze the effects of the variables Age, Prior, DiagTime, Kps, and Treatment on the survival of the patients. These prognostic factors are specified in the TEST statement, and the variable Cell is specified in the STRATA statement. Graphics results are enabled through ODS with the specification of the ODS GRAPHICS ON statement. Graphical display of the product-limit estimates (S), the negative log estimates (LS), and the log of negative log estimates (LLS) are requested through the PLOTS= option in the PROC LIFETEST statement. Because of a few large survival times, a MAXTIME of 600 is used to set the scale of the time axis; that is, the time scale extends from 0 to a maximum of 600 days in the plots. The variable Therapy is specified in the ID statement to identify the type of therapy for each observation in the product-limit estimates. The OUTTEST option specifies the creation of an output data set named Test to contain the rank test matrices for the covariates.

```
ods graphics on;
proc lifetest data=VALung plots=(s,ls,lls) outtest=Test maxtime=600;
   time SurvTime*Censor(1);
   id Therapy;
   strata Cell;
   test Age Prior DiagTime Kps Treatment;
run;
ods graphics off;
```

Output 49.1.1 through Output 49.1.4 display the product-limit estimates of the survivor functions for the four cell types. Summary statistics of the survival times are also shown. The median survival times are 51 days, 156 days, 51 days, and 118 days for patients with adeno cells, large cells, small cells, and squamous cells, respectively.

Output 49.1.1 Estimation Results for Cell=adeno

		The LIFE	ETEST Proced	lure		
		Stratum 1	l: Cell = ad	leno		
	1	Product-Limit	Survival E	stimates		
			Survival			
	Gi1	Wa di Lawa	Standard	Number	Number	m1
urvTime	Survival	Failure	Error	Failed	Left	Therapy
0.000	1.0000	0	0	0	27	
3.000	0.9630	0.0370	0.0363	1	26	standard
7.000	0.9259	0.0741	0.0504	2	25	test
8.000				3	24	standard
8.000	0.8519	0.1481	0.0684	4	23	test
12.000	0.8148	0.1852	0.0748	5	22	standard
18.000	0.7778	0.2222	0.0800	6	21	test
19.000	0.7407	0.2593	0.0843	7	20	test
24.000	0.7037	0.2963	0.0879	8	19	test
31.000	0.6667	0.3333	0.0907	9	18	test
35.000	0.6296	0.3704	0.0929	10	17	standard
36.000	0.5926	0.4074	0.0946	11	16	test
45.000	0.5556	0.4444	0.0956	12	15	test
48.000	0.5185	0.4815	0.0962	13	14	test
51.000	0.4815	0.5185	0.0962	14	13	test
52.000	0.4444	0.5556	0.0956	15	12	test
73.000	0.4074	0.5926	0.0946	16	11	test
80.000	0.3704	0.6296	0.0929	17	10	test
83.000*	•	•	•	17	9	test
84.000	0.3292	0.6708	0.0913	18	8	test
90.000	0.2881	0.7119	0.0887	19	7	test
92.000	0.2469	0.7531	0.0850	20	6	standard
95.000	0.2058	0.7942	0.0802	21	5	standard
117.000	0.1646	0.8354	0.0740	22	4	standard
132.000	0.1235	0.8765	0.0659	23	3	standard
140.000	0.0823	0.9177	0.0553	24	2	test
162.000	0.0412	0.9588	0.0401	25 26	1	standard
186.000	0	1.0000	•	26	0	test

Output 49.1.2 Estimation Results for Cell=large

The LIFETEST Procedure

Stratum 2: Cell = large

Product-Limit Survival Estimates

			Survival			
			Standard	Number	Number	
SurvTime	Survival	Failure	Error	Failed	Left	Therapy
			_	_		
0.000	1.0000	0	0	0	27	
12.000	0.9630	0.0370	0.0363	1	26	standard
15.000	0.9259	0.0741	0.0504	2	25	test
19.000	0.8889	0.1111	0.0605	3	24	test
43.000	0.8519	0.1481	0.0684	4	23	test
49.000	0.8148	0.1852	0.0748	5	22	test
52.000	0.7778	0.2222	0.0800	6	21	test
53.000	0.7407	0.2593	0.0843	7	20	test
100.000	0.7037	0.2963	0.0879	8	19	standard
103.000	0.6667	0.3333	0.0907	9	18	standard
105.000	0.6296	0.3704	0.0929	10	17	standard
111.000	0.5926	0.4074	0.0946	11	16	test
133.000	0.5556	0.4444	0.0956	12	15	test
143.000	0.5185	0.4815	0.0962	13	14	standard
156.000	0.4815	0.5185	0.0962	14	13	standard
162.000	0.4444	0.5556	0.0956	15	12	standard
164.000	0.4074	0.5926	0.0946	16	11	test
177.000	0.3704	0.6296	0.0929	17	10	standard
182.000*				17	9	standard
200.000	0.3292	0.6708	0.0913	18	8	standard
216.000	0.2881	0.7119	0.0887	19	7	standard
231.000	0.2469	0.7531	0.0850	20	6	test
250.000	0.2058	0.7942	0.0802	21	5	standard
260.000	0.1646	0.8354	0.0740	22	4	standard
278.000	0.1235	0.8765	0.0659	23	3	standard
340.000	0.0823	0.9177	0.0553	24	2	test
378.000	0.0412	0.9588	0.0401	25	1	test
553.000	0	1.0000		26	0	standard

NOTE: The marked survival times are censored observations.

Output 49.1.3 Estimation Results for Cell=small

TT'	he	नजा.ा	TEST.	Proce	dure

Stratum 3: Cell = small

Product-Limit Survival Estimates

		Product-Limit	Survival	Estimates		
			Survival			
			Standard	Number	Number	
SurvTime	Survival	Failure	Error	Failed	Left	Therapy
0.000	1.0000	0	0	0	48	
2.000	0.9792	0.0208	0.0206	1	47	test
4.000	0.9583	0.0417	0.0288	2	46	standard
7.000				3	45	standard
7.000	0.9167	0.0833	0.0399	4	44	test
8.000	0.8958	0.1042	0.0441	5	43	test
10.000	0.8750	0.1250	0.0477	6	42	standard
13.000				7	41	standard
13.000	0.8333	0.1667	0.0538	8	40	test
16.000	0.8125	0.1875	0.0563	9	39	standard
18.000				10	38	standard
18.000	0.7708	0.2292	0.0607	11	37	standard
20.000				12	36	standard
20.000	0.7292	0.2708	0.0641	13	35	test
21.000				14	34	standard
21.000	0.6875	0.3125	0.0669	15	33	test
22.000	0.6667	0.3333	0.0680	16	32	standard
24.000	0.6458	0.3542	0.0690	17	31	test
25.000				18	30	test
25.000	0.6042	0.3958	0.0706	19	29	test
27.000	0.5833	0.4167	0.0712	20	28	standard
29.000	0.5625	0.4375	0.0716	21	27	test
30.000	0.5417	0.4583	0.0719	22	26	standard
31.000	0.5208	0.4792	0.0721	23	25	standard
51.000			•	24	24	standard
51.000	0.4792	0.5208	0.0721	25	23	test
52.000	0.4583	0.5417	0.0719	26	22	standard
54.000			•	27	21	standard
54.000	0.4167	0.5833	0.0712	28	20	standard
56.000	0.3958	0.6042	0.0706	29	19	standard
59.000	0.3750	0.6250	0.0699	30	18	standard
61.000	0.3542	0.6458	0.0690	31	17	test
63.000	0.3333	0.6667	0.0680	32	16	standard
80.000	0.3125	0.6875	0.0669	33	15	test
87.000	0.2917	0.7083	0.0656	34	14	test
95.000	0.2708	0.7292	0.0641	35	13	test
97.000*	•	•	•	35	12	standard
99.000	•	•	•	36	11	test
99.000	0.2257	0.7743	0.0609	37	10	test
103.000*	•	•	•	37	9	test
117.000	0.2006	0.7994	0.0591	38	8	standard
122.000	0.1755	0.8245	0.0567	39	7	standard
123.000*	•	•	•	39	6	standard
139.000	0.1463	0.8537	0.0543	40	5	standard
151.000	0.1170	0.8830	0.0507	41	4	standard
153.000	0.0878	0.9122	0.0457	42	3	standard
287.000	0.0585	0.9415	0.0387	43	2	standard
384.000	0.0293	0.9707	0.0283	44	1	standard
392.000	0	1.0000	•	45	0	standard

NOTE: The marked survival times are censored observations.

Output 49.1.4 Estimation Results for Cell=squamous

		The LIFE	TEST Proced	ure					
		Stratum 4:	Cell = squ	amous					
		Product-Limit	Survival E	stimates					
Survival									
			Standard	Number	Number				
SurvTime	Survival	Failure	Error	Failed	Left	Therapy			
0.000	1.0000	0	0	0	35				
1.000		•		1	34	test			
1.000	0.9429	0.0571	0.0392	2	33	test			
8.000	0.9143	0.0857	0.0473	3	32	standard			
10.000	0.8857	0.1143	0.0538	4	31	standard			
11.000	0.8571	0.1429	0.0591	5	30	standard			
15.000	0.8286	0.1714	0.0637	6	29	test			
25.000	0.8000	0.2000	0.0676	7	28	test			
25.000*				7	27	standard			
30.000	0.7704	0.2296	0.0713	8	26	test			
33.000	0.7407	0.2593	0.0745	9	25	test			
42.000	0.7111	0.2889	0.0772	10	24	standard			
44.000		0.3185	0.0794		23	test			
72.000	0.6519		0.0813		22	standard			
82.000		0.3778	0.0828	13	21	standard			
87.000*				13	20	test			
100.000*				13	19	standard			
110.000	0.5895	0.4105	0.0847		18	standard			
111.000	0.5567		0.0861		17	test			
112.000	0.5240	0.4760	0.0870	16	16	test			
118.000	0.4912	0.5088	0.0875	17	15	standard			
126.000	0.4585	0.5415	0.0876	18	14	standard			
144.000	0.4257	0.5743	0.0873		13	standard			
201.000	0.3930	0.6070	0.0865	20	12	test			
228.000	0.3602		0.0852	21	11	standard			
231.000*	0 2242	0 6759	. 0940	21	10	test			
242.000	0.3242	0.6758	0.0840	22	9	test			
283.000	0.2882	0.7118	0.0820	23	8	test			
314.000	0.2522	0.7478	0.0793	24	7	standard			
357.000	0.2161		0.0757	25	6	test			
389.000	0.1801	0.8199	0.0711	26	5	test			
411.000	0.1441	0.8559	0.0654	27	4	standard			
467.000	0.1081	0.8919	0.0581	28	3	test			
587.000	0.0720	0.9280	0.0487	29	2	test			
991.000	0.0360	0.9640	0.0352	30	1	test			
999.000	0	1.0000		31	0	test			

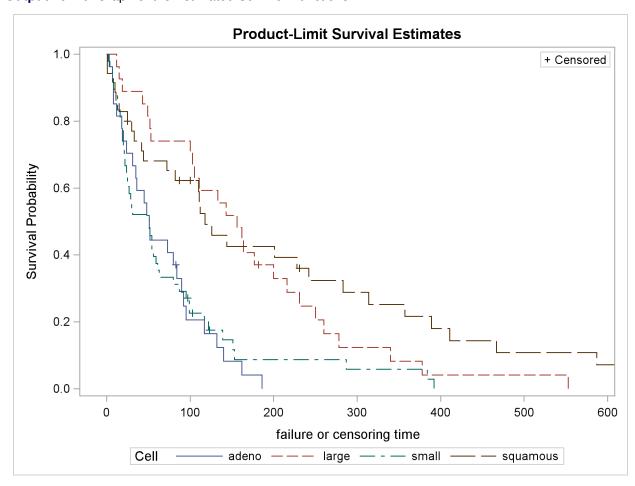
The distribution of event and censored observations among the four cell types is summarized in Output 49.1.5.

Output 49.1.5 Summary of Censored and Uncensored Values

Summa	ry of the Numb	er of Cer	sored and	Uncensored	Values
					Percent
Stratum	Cell	Total	Failed	Censored	Censored
1	adeno	27	26	1	3.70
2	large	27	26	1	3.70
3	small	48	45	3	6.25
4	squamous	35	31	4	11.43
Total		137	128	9	6.57

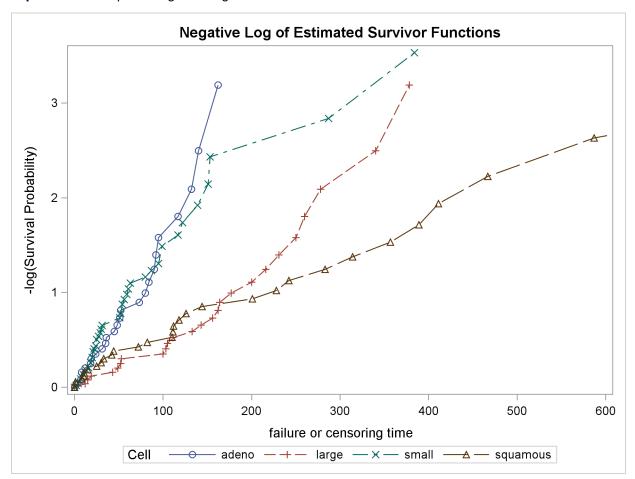
The graph of the estimated survivor functions is shown in Output 49.1.6. The adeno cell curve and the small cell curve are much closer to each other than they are to the large cell curve or the squamous cell curve. The survival rates of the adeno cell patients and the small cell patients decrease rapidly to approximately 29% in 90 days. Shapes of the large cell curve and the squamous cell curve are quite different, although both decrease less rapidly than those of the adeno and small cells. The squamous cell curve decreases more rapidly initially than the large cell curve, but the role is reversed in the later period.

Output 49.1.6 Graph of the Estimated Survivor Functions



The graph of the negative log of the estimated survivor functions is displayed in Output 49.1.7. Output 49.1.8 displays the log of the negative log of the estimated survivor functions against the log of time.

Output 49.1.7 Graph of Negative Log of the Estimated Survivor Functions



Output 49.1.8 Graph of Log of the Negative Log of the Estimated Survivor Functions

Results of the homogeneity tests across cell types are given in Output 49.1.9. The log-rank and Wilcoxon statistics and their corresponding covariance matrices are displayed. Also given is a table that consists of the approximate chi-square statistics, degrees of freedom, and p-values for the log-rank, Wilcoxon, and likelihood ratio tests. All three tests indicate strong evidence of a significant difference among the survival curves for the four types of cancer cells (p<0.0001).

Output 49.1.9 Homogeneity Tests across Cell Types

Rank Statistics						
	Cell	Log-Rank	Wilcoxon			
	adeno	10.306	697.0			
	large	-8.549	-1085.0			
	small	14.898	1278.0			
	squamous	-16.655	-890.0			

Output 49.1.9 continued

1	Covariance M	atrix for the	Log-Ra	ank Statistics	
Cell	aden	o lar	ge	small	squamous
adeno	12.966	2 -4.07	01	-4.4087	-4.4873
large	-4.070	1 24.19	90	-7.8117	-12.3172
small	-4.408	7 -7.81	17	21.7543	-9.5339
squamous	-4.487	3 –12.31	72	-9.5339	26.3384
1	Covariance M	atrix for the	Wilcox	on Statistics	
Cell	aden	o lar	ge	small	squamous
adeno	12118	8 -347	18	-46639	-39831
large	-3471	8 1512	41	-59948	-56576
small	-4663	9 –599	48	175590	-69002
squamous	-3983	1 -565	76	-69002	165410
	Tes	t of Equality	over S	Strata	
				Pr >	
	Test	Chi-Square	DF	Chi-Square	
	Log-Rank	25.4037	3	<.0001	
	Wilcoxon	19.4331	3	0.0002	
	-2Log(LR)	33.9343	3	<.0001	

Results of the log-rank test of the prognostic variables are shown in Output 49.1.10. The univariate test results correspond to testing each prognostic factor marginally. The joint covariance matrix of these univariate test statistics is also displayed. In computing the overall chi-square statistic, the partial chi-square statistics following a forward stepwise entry approach are tabulated.

Consider the log-rank test in Output 49.1.10. Since the univariate test for Kps has the largest chi-square (43.4747) among all the covariates, Kps is entered first. At this stage, the partial chi-square and the chi-square increment for Kps are the same as the univariate chi-square. Among all the covariates not in the model (Age, Prior, DiagTime, Treatment), Treatment has the largest approximate chi-square increment (1.7261) and is entered next. The approximate chi-square for the model containing Kps and Treatment is 43.4747+1.7261=45.2008 with 2 degrees of freedom. The third covariate entered is Age. The fourth is Prior, and the fifth is DiagTime. The overall chi-square statistic in the last line of the output is the partial chi-square for including all the covariates. It has a value of 46.4200 with 5 degrees of freedom, which is highly significant (p<0.0001).

Output 49.1.10 Log-Rank Test of the Prognostic Factors

	Univ	ariate Chi	Squares	for the Log-	Rank Test	
	Test	Standard		Pr >		
Variable	Statistic	Error	Chi-Squa	re Chi-Square	Label	
Age	-40.7383	105.7	0.148	5 0.7000	age in years	
Prior	-19.9435	46.9836	0.180	2 0.6712		
DiagTime	-115.9	97.8708	1.401	3 0.2365	months till :	randomization
Kps	1123.1	170.3	43.474	7 <.0001	karnofsky in	dex
Treatment	-4.2076	5.0407	0.696	7 0.4039	treatment in	dicator
	Cova	riance Mat	rix for	the Log-Rank	Statistics	
Variable	A	.ge	Prior	DiagTime	Kps	Treatment
Age	11175	. 4	-301.2	-892.2	-2948.4	119.3
Prior	-301	2	2207.5	2010.9	78.6	13.9
DiagTime	-892	2	2010.9	9578.7	-2295.3	21.9
Kps	-2948	. 4	78.6	-2295.3	29015.6	61.9
KPS	2340		70.0	2233.3	23020.0	01.5
Treatment	119		13.9	21.9	61.9	
Treatment	119	.3	13.9	21.9		25.4
Treatment	119	.3	13.9	21.9	61.9	25.4
Treatment	119 orward Step	.3 owise Seque	13.9	21.9 hi-Squares fo	61.9	25.4 k Test
Treatment F	119 orward Step	.3 wise Seque	13.9	21.9 hi-Squares fo	61.9 r the Log-Ran Chi-Square	25.4 k Test Pr >
Treatment F Variab	119 orward Step le DF	.3 www.se Seque Chi-Sc	13.9 ence of C	21.9 hi-Squares fo Pr > Chi-Square	61.9 or the Log-Ran Chi-Square Increment	25.4 k Test Pr > Increment
Treatment F Variab Kps	119 orward Step le DF	Chi-Sc 43.4	13.9 ence of Conguere	21.9 hi-Squares fo Pr > Chi-Square <.0001	61.9 or the Log-Ran Chi-Square Increment 43.4747	25.4 k Test Pr > Increment <.0001
Treatment F Variab Kps Treatm	119 orward Step le DF 1 ent 2	Chi-Sc 43.4 45.2 46.3	13.9 ence of C quare 1747 2008	21.9 hi-Squares fo Pr > Chi-Square <.0001 <.0001	61.9 or the Log-Ran Chi-Square Increment 43.4747 1.7261	25.4 k Test Pr > Increment <.0001 0.1889
Treatment F Variab Kps Treatm Age	orward Step le DF lent 2 3 4	Chi-Sc 43.4 45.2 46.3 46.4	13.9 ence of C quare 1747 2008 8012	21.9 hi-Squares for Pr > Chi-Square <.0001 <.0001	61.9 or the Log-Ran Chi-Square Increment 43.4747 1.7261 1.1004	25.4 k Test Pr > Increment <.0001 0.1889 0.2942
Treatment F Variab Kps Treatm Age Prior	orward Step le DF ent 2 and 4 me 5	Chi-Sc 43.4 45.2 46.3 46.4	13.9 ence of C quare 1747 2008 8012 1134	21.9 hi-Squares for Pr > Chi-Square	61.9 or the Log-Ran Chi-Square Increment 43.4747 1.7261 1.1004 0.1122	25.4 k Test Pr > Increment <.0001 0.1889 0.2942 0.7377
Treatment F Variab Kps Treatm Age Prior	119 forward Step le DF lent 2 3 4 me 5	Chi-Sc. 43.4 45.2 46.3 46.4 46.4	13.9 ence of C quare 1747 2008 3012 1134 1200 Label	21.9 hi-Squares for Pr > Chi-Square	61.9 or the Log-Ran Chi-Square Increment 43.4747 1.7261 1.1004 0.1122	25.4 k Test Pr > Increment <.0001 0.1889 0.2942 0.7377
Treatment F Variab Kps Treatm Age Prior	119 forward Step le DF lent 2 3 4 me 5	Chi-Sc. 43.4 45.2 46.3 46.4 Variable	13.9 ence of C quare 1747 2008 3012 1134 1200 Label karno	21.9 hi-Squares for Pr > Chi-Square <.0001 <.0001 <.0001 <.0001 <.0001	61.9 or the Log-Ran Chi-Square Increment 43.4747 1.7261 1.1004 0.1122 0.00665	25.4 k Test Pr > Increment <.0001 0.1889 0.2942 0.7377
Treatment F Variab Kps Treatm Age Prior	orward Step le DF ment 2 3 4 me 5	Chi-Sc 43.4 45.2 46.4 Variable Kps Treatment Age	13.9 ence of C quare 4747 2008 3012 4134 4200 Label karno treat	21.9 hi-Squares for Pr > Chi-Square <.0001 <.0001 <.0001 <.0001 <.0001	61.9 or the Log-Ran Chi-Square Increment 43.4747 1.7261 1.1004 0.1122 0.00665	25.4 k Test Pr > Increment <.0001 0.1889 0.2942 0.7377
Treatment F Variab Kps Treatm Age Prior	orward Step le DF ment 2 3 4 me 5	Chi-Sc 43.4 45.2 46.4 Variable Kps Treatment	13.9 ence of C quare 1747 2008 2012 1134 2200 Label karno treat: age i prior	21.9 hi-Squares for Pr > Chi-Square <.0001 <.0001 <.0001 <.0001 fsky index ment indicato	61.9 or the Log-Rand Chi-Square Increment 43.4747 1.7261 1.1004 0.1122 0.00665	25.4 k Test Pr > Increment <.0001 0.1889 0.2942 0.7377

You can establish this forward stepwise entry of prognostic factors by passing the matrix corresponding to the log-rank test to the RSQUARE method in the REG procedure, as follows. PROC REG finds the sets of variables that yield the largest chi-square statistics.

Output 49.1.11 displays the univariate statistics and their covariance matrix for the log-rank test.

Output 49.1.11 Log-Rank Statistics and Covariance Matrix

		All Possil	ole Subset	s of Covar	iates for	r the log-	rank Test	
0bs	_TYPE_	_NAME_	SurvTime	Age	Prior	DiagTime	Kps	Treatment
1	cov	SurvTime	46.42	-40.74	-19.94	-115.86	1123.14	-4.208
2	cov	Age	-40.74	11175.44	-301.23	-892.24	-2948.45	119.297
3	cov	Prior	-19.94	-301.23	2207.46	2010.85	78.64	13.875
4	cov	DiagTime	-115.86	-892.24	2010.85	9578.69	-2295.32	21.859
5	cov	Kps	1123.14	-2948.45	78.64	-2295.32	29015.62	61.945
6	cov	Treatment	-4.21	119.30	13.87	21.86	61.95	25.409

Results of the best subset regression are shown in Output 49.1.12. The variable Kps generates the largest univariate test statistic among all the covariates, the pair Kps and Age generate the largest test statistic among any other pairs of covariates, and so on. The entry order of covariates is identical to that of PROC LIFETEST.

Output 49.1.12 Best Subset Regression from the REG Procedure

		REG Procedure
		Model: MODEL1
	Dependent	Variable: SurvTime
	R-Squar	re Selection Method
Number in		
Model	R-Square	Variables in Model
1	0.9366	Kps
1	0.0302	DiagTime
1	0.0150	_
1	0.0039	Prior
1	0.0032	Age
2	0.9737	Kps Treatment
2	0.9472	Age Kps
2		Prior Kps
2	0.9382	DiagTime Kps
2	0.0434	
2		Age DiagTime
2		Prior DiagTime
2		Prior Treatment
2	0.0159	
2	0.0075	Age Prior
3	0.9974	Age Kps Treatment
3	0.9774	Prior Kps Treatment
3		DiagTime Kps Treatment
3	0.9515	Age Prior Kps
3	0.9481	Age DiagTime Kps
3		Prior DiagTime Kps
3		Age DiagTime Treatment
3		Prior DiagTime Treatment
3		Age Prior DiagTime
3	0.0192	Age Prior Treatment
4	0.9999	Age Prior Kps Treatment
4	0.9976	Age DiagTime Kps Treatment
4	0.9774	Prior DiagTime Kps Treatment
4	0.9515	Age Prior DiagTime Kps
4	0.0459	Age Prior DiagTime Treatment
5	1.0000	Age Prior DiagTime Kps Treatment

Example 49.2: Enhanced Survival Plot and Multiple-Comparison Adjustments

This example highlights some of the new features of PROC LIFETEST for SAS 9.2, especially the survival plot with number of subjects at risk and multiple comparisons of survival curves. In the following DATA step, data of 137 bone marrow transplant patients extracted from Klein and Moeschberger (1997) are saved in the data set BMT. At the time of transplant, each patient is classified into one of three risk categories: ALL (Acute Lymphoblastic Leukemia), AML (Acute Myelocytic Leukemia)-Low Risk, and AML-High Risk. The endpoint of interest is the disease-free survival time, which is the time to death or relapse or the end of the study in days. In this data set, the variable Group represents the patient's risk category, the variable T represents the disease-free survival time, and the variable Status is the censoring indicator, with the value 1 indicating an event time and the value 0 a censored time.

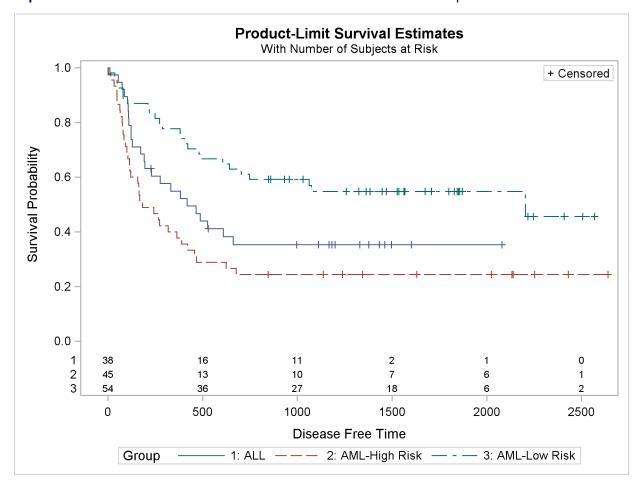
```
proc format;
  value risk 1='ALL' 2='AML-Low Risk' 3='AML-High Risk';
data BMT;
  input Group T Status @@;
  format Group risk.;
  label T='Disease Free Time';
  datalines;
1 2081 0 1 1602 0 1 1496 0 1 1462 0 1 1433 0
1 1377 0 1 1330 0 1 996 0 1 226 0 1 1199 0
1 1111 0 1 530 0 1 1182 0 1 1167 0 1 418 1
  383 1 1 276 1 1 104 1 1 609 1 1 172 1
  487 1 1 662 1 1 194 1 1 230 1 1 526 1
  122 1 1 129 1 1
                   74 1 1 122 1 1
  466 1 1 192 1 1 109 1 1
                             55 1 1
                                      1 1
  107 1 1 110 1 1 332 1 2 2569 0 2 2506 0
2 2409 0 2 2218 0 2 1857 0 2 1829 0 2 1562 0
2 1470 0 2 1363 0 2 1030 0 2 860 0 2 1258 0
2 2246 0 2 1870 0 2 1799 0 2 1709 0 2 1674 0
2 1568 0 2 1527 0 2 1324 0 2
                            957 0 2 932 0
2 847 0 2 848 0 2 1850 0 2 1843 0 2 1535 0
2 1447 0 2 1384 0 2 414 1 2 2204 1 2 1063 1
2 481 1 2 105 1 2 641 1 2 390 1 2 288 1
  421 1 2
          79 1 2 748 1 2 486 1 2
                                      48 1
2 272 1 2 1074 1 2 381 1 2
                            10 1 2
                                      53 1
   80 1 2
          35 1 2 248 1 2 704 1 2 211 1
2 219 1 2 606 1 3 2640 0 3 2430 0 3 2252 0
3 2140 0 3 2133 0 3 1238 0 3 1631 0 3 2024 0
3 1345 0 3 1136 0 3 845 0 3 422 1 3 162 1
3
   84 1 3 100 1 3 2 1 3
                             47 1 3 242 1
  456 1 3 268 1 3 318 1 3
                             32 1 3 467 1
   47 1 3 390 1 3 183 1 3 105 1 3 115 1
3 164 1 3
          93 1 3 120 1 3 80 1 3 677 1
   64 1 3 168 1 3 74 1 3 16 1 3 157 1
3 625 1 3
           48 1 3 273 1 3
                             63 1 3
                                    76 1
3 113 1 3 363 1
```

In the following statements, PROC LIFETEST is invoked to compute the product-limit estimate of the survivor function for each risk category. Using ODS Graphics, you can display the number of subjects at risk in the survival plot. The PLOTS= option requests that the survival curves be plotted, and the ATRISK= suboption specifies the time points at which the at-risk numbers are displayed. In the STRATA statement, the ADJUST=SIDAK option requests the Šidák multiple-comparison adjustment, and by default, all paired comparisons are carried out.

```
ods graphics on;
proc lifetest data=BMT plots=survival(atrisk=0 to 2500 by 500);
  time T * Status(0);
  strata Group / test=logrank adjust=sidak;
  run;
```

Output 49.2.1 displays the estimated disease free survival for the three leukemia groups with the number of subjects at risk at 0, 500, 1000, 1500, 2000, and 2500 days. Patients in the AML-Low Risk group experience disease free longer than those in the ALL group, who in turn fare better than those in the AML-High Risk group.

Output 49.2.1 Estimated Disease-Free Survival for 137 Bone Marrow Transplant Patients



The log-rank test (Output 49.2.2) shows that the disease-free survival times for these three risk groups are significantly different (p=0.001).

Output 49.2.2 Log-Rank Test of Disease Group Homogeneity

```
Test of Equality over Strata

Pr >

Test Chi-Square DF Chi-Square

Log-Rank 13.8037 2 0.0010
```

The Šidák multiple-comparison results are shown in Output 49.2.3. There is no significant difference in disease-free survivor functions between the ALL and AML-High Risk groups (p=0.2779). The difference between the ALL and AML-Low Risk groups is marginal (p=0.0685), but the AML-Low Risk and AML-High Risk groups have significantly different disease-free survivor functions (p=0.0006).

Output 49.2.3 All Paired Comparsions

Strata C	omparison		p-Va	lues
Group	Group	Chi-Square	Raw	Sidak
ALL	AML-High Risk	2.6610	0.1028	0.2779
ALL	AML-Low Risk	5.1400	0.0234	0.0685
AML-High Risk	AML-Low Risk	13.8011	0.0002	0.0006

Suppose you consider the AML-Low Risk group as the reference group. You can use the DIFF= option in the STRATA statement to designate this risk group as the control and apply a multiple-comparison adjustment to the *p*-values for the paired comparison between the AML-Low Risk group with each of the other groups. Consider the Šidák correction again. You specify the ADJUST= and DIFF= options as in the following statements.

```
proc lifetest data=BMT notable plots=none;
  time T * Status(0);
  strata Group / test=logrank adjust=sidak diff=control('AML-Low Risk');
  run;
```

Output 49.2.4 shows that although both the ALL and AML-High Risk groups differ from the AML-Low Risk group at the 0.05 level, the difference between the AML-High Risk and the AML-Low Risk group is highly significant (p=0.0004).

Output 49.2.4 Comparisons with the Reference Group

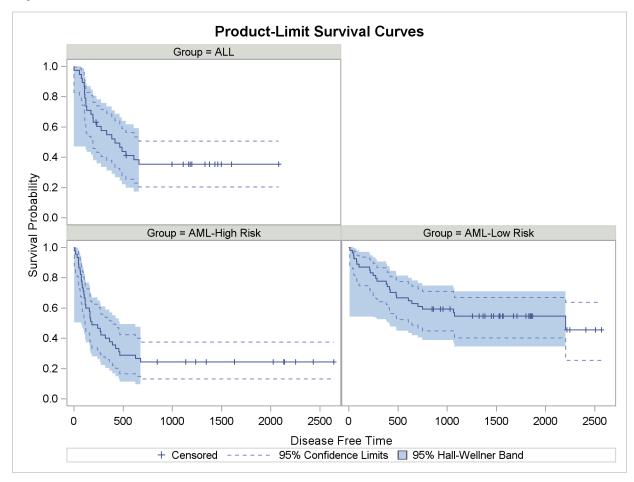
	The	LIFETES	T Procedure		
Adjustment	for Multip	ole Comp	arisons for th	e Logrank	Test
Strata C	omparison			p-Va	lues
Group		Group	Chi-Square	Raw	Sidak
ALL	AML-Low	Risk	5.1400	0.0234	0.0462
AML-High Risk	AML-Low	Risk	13.8011	0.0002	0.0004

Klein and Moeschberger (1997, Section 4.4) describe in detail how to compute the Hall-Wellner (HW) and equal-precision (EP) confidence bands for the survivor function. You can output these simultaneous confidence intervals to a SAS data set by using the CONFBAND= and OUTSURV= options in the PROC LIFETEST statement. You can display survival curves with pointwise and simultaneous confidence limits through ODS Graphics. When the survival data are stratified, displaying all the survival curves and their confidence limits in the same plot can make the plot appear cluttered. In the following statements, the PLOTS= specification requests that the survivor functions be displayed along with their pointwise confidence limits (CL) and Hall-Wellner confidence bands (CB=HW). The STRATA=PANEL specification requests that the survival curves be displayed in a panel of three plots, one for each risk group.

```
proc lifetest data=BMT plots=survival(cl cb=hw strata=panel);
   time T * Status(0);
   strata Group;
   run;
ods graphics off;
```

The panel plot is shown in Output 49.2.5.

Output 49.2.5 Estimated Disease-Free Survivor Functions with Confidence Limits



Example 49.3: Life-Table Estimates for Males with Angina Pectoris

The data in this example come from Lee (1992, p. 91) and represent the survival rates of males with angina pectoris. Survival time is measured as years from the time of diagnosis. In the following DATA step, the data are read as number of events and number of withdrawals in each one-year time interval for 16 intervals. Three variables are constructed from the data: Years (an artificial time variable with values that are the midpoints of the time intervals), Censored (a censoring indicator variable with the value 1 indicating censored observations and the value 0 indicating event observations), and Freq (the frequency variable). Two observations are created for each interval, one representing the event observations and the other representing the censored observations.

```
title 'Survival of Males with Angina Pectoris';
data Males;
  keep Freq Years Censored;
  retain Years -.5;
  input fail withdraw @@;
  Years + 1;
  Censored=0;
  Freq=fail;
  output;
  Censored=1;
  Freq=withdraw;
  output;
  datalines;
456 0 226 39 152 22 171 23 135 24 125 107
 83 133 74 102 51 68 42 64 43 45 34 53
 18 33 9 27 6 23 0 30
```

In the following statements, the ODS GRAPHICS ON specification enables ODS Graphics. PROC LIFETEST is invoked to compute the various life-table survival estimates, the median residual time, and their standard errors. The life-table method of computing estimates is requested by specifying METHOD=LT. The intervals are specified by the INTERVAL= option. Graphical display of the life-table survivor function estimate, negative log of the estimate, log of negative log of the estimate, estimated density function, and estimated hazard function are requested by the PLOTS= option. No tests for homogeneity are carried out because the data are not stratified.

Results of the life-table estimation are shown in Output 49.3.1. The five-year survival rate is 0.5193 with a standard error of 0.0103. The estimated median residual lifetime, which is 5.33 years initially, reaches a maximum of 6.34 years at the beginning of the second year and decreases gradually to a value lower than the initial 5.33 years at the beginning of the seventh year.

Output 49.3.1 Life-Table Survivor Function Estimate

Survival of Males with Angina Pectoris

The LIFETEST Procedure

Life Table Survival Estimates

Inter	rval	Number	Number	Effective Sample	Conditional Probability	Conditional Probability Standard
[Lower,	Upper)	Failed	Censored	Size	of Failure	Error
0	1	456	0	2418.0	0.1886	0.00796
1	2	226	39	1942.5	0.1163	0.00728
2	3	152	22	1686.0	0.0902	0.00698
3	4	171	23	1511.5	0.1131	0.00815
4	5	135	24	1317.0	0.1025	0.00836
5	6	125	107	1116.5	0.1120	0.00944
6	7	83	133	871.5	0.0952	0.00994
7	8	74	102	671.0	0.1103	0.0121
8	9	51	68	512.0	0.0996	0.0132
9	10	42	64	395.0	0.1063	0.0155
10	11	43	45	298.5	0.1441	0.0203
11	12	34	53	206.5	0.1646	0.0258
12	13	18	33	129.5	0.1390	0.0304
13	14	9	27	81.5	0.1104	0.0347
14	15	6	23	47.5	0.1263	0.0482
15	٠	0	30	15.0	0	0

				Survival	Median	Median
Inte	rval			Standard	Residual	Standard
[Lower,	Upper)	Survival	Failure	Error	Lifetime	Error
0	1	1.0000	0	0	5.3313	0.1749
1	2	0.8114	0.1886	0.00796	6.2499	0.2001
2	3	0.7170	0.2830	0.00918	6.3432	0.2361
3	4	0.6524	0.3476	0.00973	6.2262	0.2361
4	5	0.5786	0.4214	0.0101	6.2185	0.1853
5	6	0.5193	0.4807	0.0103	5.9077	0.1806
6	7	0.4611	0.5389	0.0104	5.5962	0.1855
7	8	0.4172	0.5828	0.0105	5.1671	0.2713
8	9	0.3712	0.6288	0.0106	4.9421	0.2763
9	10	0.3342	0.6658	0.0107	4.8258	0.4141
10	11	0.2987	0.7013	0.0109	4.6888	0.4183
11	12	0.2557	0.7443	0.0111		
12	13	0.2136	0.7864	0.0114	•	
13	14	0.1839	0.8161	0.0118	•	
14	15	0.1636	0.8364	0.0123		

Output 49.3.1 continued

	Su	rvival	of Mal	es with An	gina Pe	ctoris		
		Т	he LIF	ETEST Proc	edure			
Interva	al Upper)	Survi	val	Failure	Surviv Standa Error		edian sidual fetime	
15		0.1	429	0.8571	0.01	33		
[Lower,		per)	PDF	Erro		Hazard	Erro	
(0	1	0.18	86 0.00	796 0	.208219	0.009	0698
1	1	2	0.09	0.00	598 0	.123531	0.008	3201
2	2	3	0.06	46 0.00	507	0.09441	0.007	649
3	3	4	0.07	38 0.00	543 0	.119916	0.009	154
4	4	5	0.05			.108043		
	5	6				.118596		
	6	7	0.04			0.1		
	7	8				.116719		
	3	9				0.10483		
	9	10				.112299		
1(11		11 12				.155235 0.17942		
12		13				0.17942 .149378		
13		14				.116883		
		15	0.02			.134831		
14								

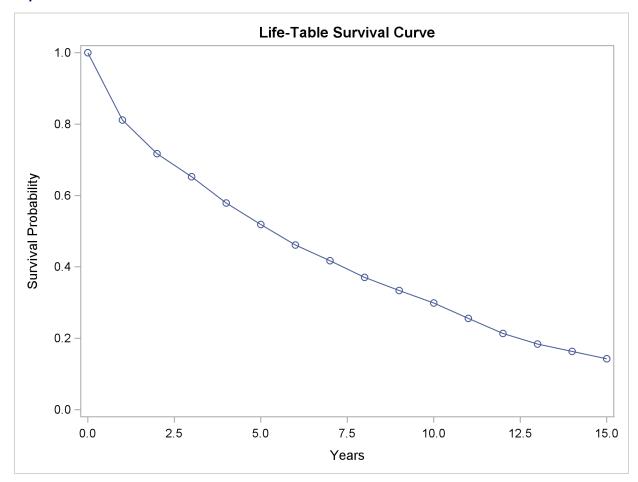
The breakdown of event and censored observation in the data is shown in Output 49.3.2. Note that 32.8% of the patients have withdrawn from the study.

Output 49.3.2 Summary of Censored and Event Observations

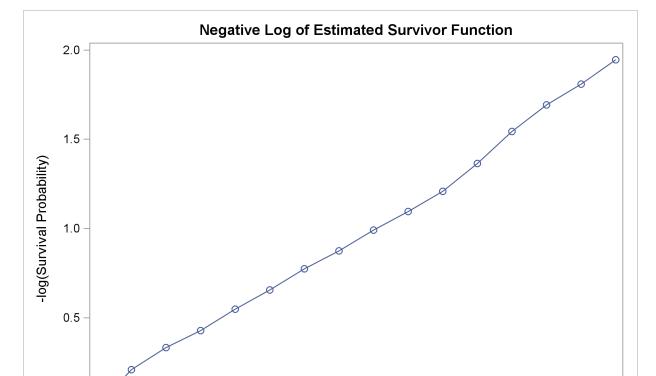
Summary of th	e Number	of Censored and	Uncensored Value	ues
			Percent	
Tot	al Faile	d Censored	Censored	
24	18 162	5 793	32.80	
NOTE: 2 observations wit	h invalid	time, censoring deleted.	g, or frequency	values were

Output 49.3.3 displays the graph of the life-table survivor function estimate. The median survival time, read from the survivor function curve, is 5.33 years, and the 25th and 75th percentiles are 1.04 and 11.13 years, respectively.

Output 49.3.3 Life-Table Survivor Function Estimate



An exponential model might be appropriate for the survival of these male patients with angina pectoris since the curve of the negative log of the survivor function estimate versus the survival time (Output 49.3.4) approximates a straight line through the origin. Note that the graph of the log of the negative log of the survivor function estimate versus the log of time (Output 49.3.5) is practically a straight line.



Output 49.3.4 Negative Log of Survivor Function Estimate

0.0

0.0

2.5

As discussed in Lee (1992), the graph of the estimated hazard function (Output 49.3.6) shows that the death rate is highest in the first year of diagnosis. From the end of the first year to the end of the tenth year, the death rate remains relatively constant, fluctuating between 0.09 and 0.12. The death rate is generally higher after the tenth year. This could indicate that a patient who has survived the first year has a better chance than a patient who has just been diagnosed. The profile of the median residual lifetimes also supports this interpretation.

7.5

Years

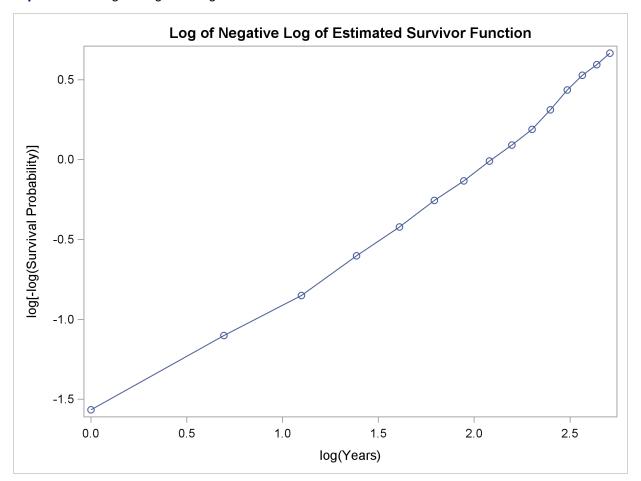
10.0

12.5

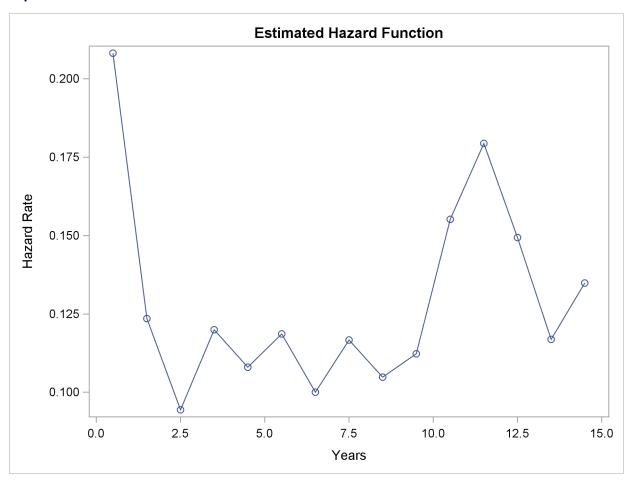
15.0

5.0

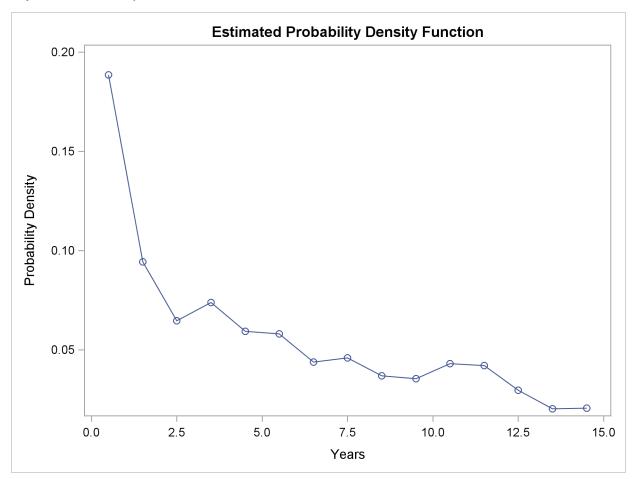
Output 49.3.5 Log of Negative Log of Survivor Function Estimate



Output 49.3.6 Hazard Function Estimate



The density estimate is shown in (Output 49.3.7). Visually, it resembles the density function of an exponential distribution.



Output 49.3.7 Density Function Estimate

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